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KERATOSIS OF THE LARYNX

Chairman's Address

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Epithelial hyperplasia of the larynx may assume all gradations from simple diffuse thickening in chronic inflammation to localized keratosis, papillomatous masses which fill the larynx or carcinomatous ulceration with extensive invasion. As a result, difficult problems in diagnosis are encountered.

Localized areas of thickening of the epithelium which appear as single or multiple chalky white elevations on the upper surface and edge of one or both vocal cords usually with involvement of the membranous portion are not uncommon. These have been designated as keratosis, hyperkeratosis, leukoplakia, pachydermia laryngis or by other terms by laryngologists and pathologists, and by some these terms appear to be used synonymously; others consider them as distinct and different entities.

Pachydermia laryngis as described by Virchow referred to thickening of the posterior wall of the larynx and the posterior half of the vocal cords. It was observed in alcoholic addicts or excessive voice users, as street hawkers. The involved areas are grayish white and exhibit proliferation of the superficial epithelium as well as thickening of the basal layers, so that the histologic appearances often suggest papilloma.

Keratosis, hyperkeratosis or leukoplakia is primarily a localized benign hyperplasia of epithelium which does not invade the submucosa. The whitish surface which may appear smooth or granular or may exhibit elevations or villous projections stands out in contrast to the surrounding cordal mucosa which often is the seat of a chronic inflammatory process.

CAUSES

The causes of keratosis are still in the realm of speculation. It is observed more commonly in male adults who are addicted to excessive smoking, particularly of cigarets. Although I am convinced that this is a predisposing factor, it is obvious that such a statement lacks definite proof. Excessive use of the voice and alcoholism do not appear as important etiologic factors. The incidence of syphilis does not appear greater among patients with keratosis. The frequent association of keratosis with chronic laryngitis suggests long-continued irritation as a predisposing cause. Studies in food deficiency diseases indicate that keratosis is often a manifestation. It has long been observed that keratinization of the skin is related to disturbances in vitamin A metabolism. Whether this is the result of an inadequate diet or failure to assimilate vitamins cannot always be accurately determined. Wolbach and Howe [1] have reported changes in epithelium which followed deprivation of fat soluble vitamin A in experimental studies on rats. These changes consisted of the substitution of stratified keratinizing epithelium for normal epithelium in various parts of the respiratory tract and elsewhere. There is clinical evidence to substantiate this view.

Graham [2] reported his observations on the effects of a high vitamin diet in a case of keratosis of the larynx. In spite of a histologic diagnosis of carcinoma there was observed remarkable regression of the entire lesion as soon as attention was paid to the patient's diet.

In discussing keratosis in general, Reimann [3] considered it "to be primarily a disease of shedding of the superficial layers. These cells do not differentiate as do normal cells but stick together, pile up and produce the islands we call keratinized because of the excess of keratin in the cells." The occasional appearance of villous projections on an area of keratosis has suggested a mycotic origin, since these appear similar to the mycelial filaments observed in infections by the leptothrix group. Histologic study of the white villi in keratosis shows cornification of epithelium. The rare occurrence of a leptothrix is an incidental observation.

Although excessive use or abuse of the voice may lead to localized keratosis seen as vocal nodules or to diffuse polypoid hyperplasia of the vocal cords, the clinical and histologic appearances are not those of keratosis (fig. 1).

While there is definite overgrowth of epithelium, the basement membrane is usually even, and the submucosal tissues exhibit little or no inflammatory reaction and are the seat of edema. In the forms of keratosis appearing on the surface of a vocal cord there is commonly observed a variable amount of inflammatory reaction in the submucosa. This has caused much comment, and the question has arisen whether it is of prognostic import. New and Erich,[4] Graham,[2] Bucher [5] and others have directed attention to this pronounced subepithelial inflammation (fig. 2).

PRECANCEROUS LESIONS

Clinical observations have long shown that many tumors arise from tissues that were once normal, and various forms of chronic inflammatory changes are

Read before the Section on Laryngology, Otology and Rhinology at the Ninety-Fifth Annual Session of the American Medical Association, San Francisco, July 4, 1946.

1. Wolbach, S. B., and Howe, P. R.: Tissue Changes Following Deprivation of Fat-Soluble A Vitamin, J. Exper. Med. **42**: 753, 1925.
2. Graham, H. B.: Keratosis of the Larynx, Arch. Otolaryng. **36**: 735 (Nov.) 1942.
3. Reimann, S. P.: Personal communication to the author.
4. New, G. B., and Erich, J. B.: Benign Tumors of the Larynx: Study of 722 Cases, Arch. Otolaryng. **28**: 841 (Dec.) 1938.
5. Bucher, C. J.: Personal communication to the author.

observed to precede the appearance of many tumors. This brings up the interesting and much debated question of whether keratosis or any form of benign epithelial hyperplasia may be considered as a so-called precancerous lesion.

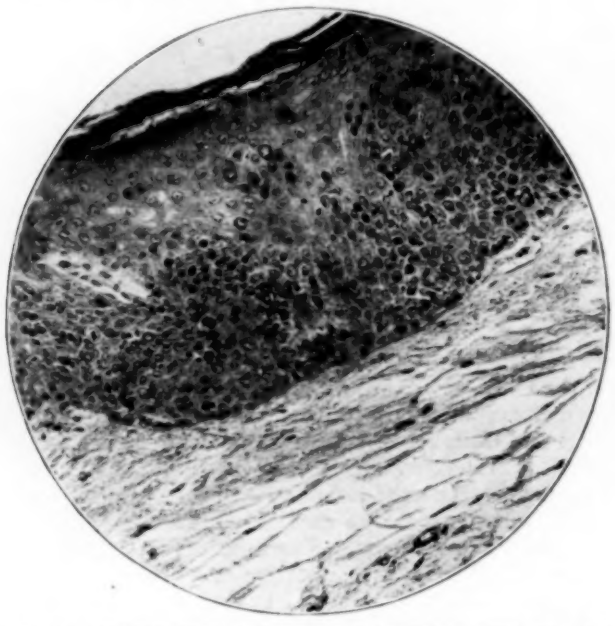

Fig. 1.—Photomicrograph (× 200) of a hyperplastic vocal cord. The epithelium is greatly thickened, but the basement membrane is regular. There is definite edema and fibrosis with a few inflammatory cells in the submucosal layer.

In chronic inflammatory lesions of the larynx in which there develops decided hyperplasia of the epithelium in an effort at repair, this hyperplasia and this irregularity frequently suggest early malignant changes. The term precancerous has been applied to this type of lesions by many writers, and there undoubtedly is some justification for its use by laryngologists when they have under consideration certain benign lesions that have undergone malignant changes. As stated by Crawford [6] "in the histologic examination of tissue in a number of these cases it was impossible to predict with any degree of certainty in which cancer would develop and in which recovery would occur." It is, of course, obvious that the pathologist cannot anticipate by a study of cells that a benign lesion will become malignant. Coplin [7] appropriately stated that "histology rarely, if ever, tells us what a cell is going to do before it does it, although many of us are constantly deluding ourselves into the belief that we can deduce the future of a cell from a study of the past or present or both."

In Graham's [2] case of keratosis there was histologic evidence of carcinoma. Morrison [8] reported a case of keratosis in which a carcinoma apparently developed as a single small island of malignant cells in the subepithelial layer beneath a mucous gland. A satisfactory result was secured by laryngofissure. New and Erich [4] reported 10 cases, in 2 of which there developed squamous cell carcinoma. The carcinomatous lesions were definitely localized in both of these cases. The carcinoma was discovered histologically, and the authors emphasized the importance of thorough microscopic examination. Eggston [9] stated that keratosis should always be considered a precancerous lesion. After many years of experience in a study of the pathologic changes observed in these cases he found in many instances that they sooner or later, after several biopsies, had grown to be frankly epidermoid carcinoma. This may occur in a matter of months or even years. He expressed his conviction that keratosis of the larynx should be treated as a precancerous lesion and preferably by surgical removal. Reimann [3] believed that many of these lesions are precancerous but that it is impossible to say which of a group of such keratoses will turn into cancer. In the interests of cancer prevention, if all keratoses were removed completely none could develop into carcinoma. While it is not known whether carcinoma develops from purely local causes or whether, in addition, there must be a constitutional or genetic influence, he stated that in the case of certain extremely powerful carcinogens, probably the local influence far outweighs any other; but in the case of keratoses in general, there is certainly a constitutional predisposition. In discussing keratosis, the Jacksons [10] stated that "so far no case has shown malignant developments."

PATHOLOGY

From the pathologist's point of view, Bucher [5] described the whitish elevations on the vocal cords as small masses of hyperplastic squamous epithelium, which at times are suggestive of papilloma, but the usual characteristic arrangement is lacking. The basement membrane is commonly regular, sometimes pushing into the submucosa in small irregular projections so that it becomes difficult to decide whether there is infiltration or whether the process is merely a part of the hyperplasia. In most instances a good basal layer of epithelium is observed. The keratinization varies

Fig. 2.—Photomicrograph (× 100) of section with definite epithelial hyperplasia and keratinization. The basement membrane lacks clear definition; the basal cells are deeply staining; the submucosal layer exhibits pronounced inflammatory changes. This type of keratosis is extremely suggestive of early carcinoma.

6. Clerf, L. H., and Crawford, B. L.: Carcinoma of the Larynx: Clinical and Pathologic Aspects, Arch. Otolaryng. **16**: 676 (Nov.) 1932.
7. Coplin, W. M. L.: A Basis for the Prevention of Cancer, J. A. M. A. **78**: 1523 (May 20) 1922.
8. Morrison, L. F.: Keratosis of the Larynx Showing Early Malignant Changes, Tr. Pacific Coast Oto-Ophth. Soc. **25**: 235, 1940.
9. Eggston, A. A.: Personal communication to the author.
10. Jackson, C., and Jackson, C. L.: Diseases and Injuries of Larynx, ed. 2, New York, The Macmillan Company, 1942.

in different persons. The changes in the submucosal tissues are important and consist in infiltration with cells of inflammatory origin (namely, lymphocytes, monocytes and plasma cells), the presence of numerous thin-walled vessels and edema with a variable amount

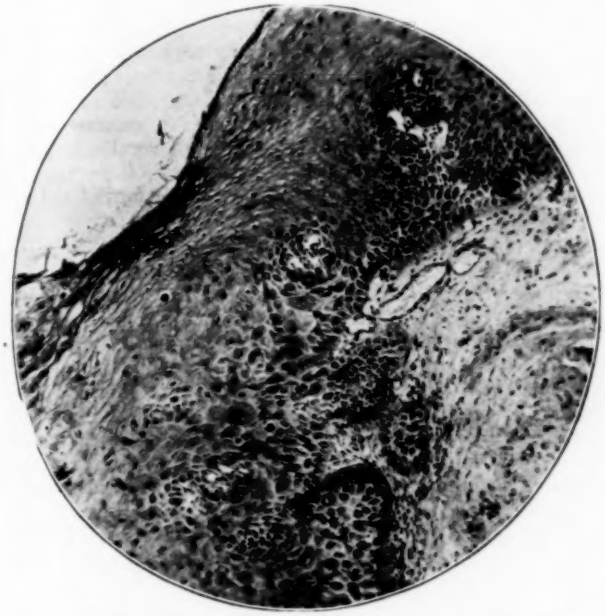

Fig. 3.—Photomicrograph (× 100) of keratotic tissue reveals thickened epithelium with projections extending into the submucosal layer. The basement membrane, however, appears intact. Moderate inflammatory changes are present in the submucosa.

of fibrosis. Occasionally there are deposits of blood pigments. The older pathologists referred to this type of keratosis as pachydermia verrucosa. In reviewing histologic slides in a large number of cases of keratosis over many years, particularly in those in which frequent biopsies have been performed, it is his belief that lesions which show considerable inflammatory changes and great irregularity of the basement membrane should be dealt with in the same manner as early carcinoma.

SYMPTOMS

Although the laryngoscopic appearances and the extent of the keratotic lesions may vary, there is commonly but one symptom, namely, change in the voice. This may consist only of slight huskiness, or the voice may be hoarse. Occasionally there may be clearing of the throat.

TREATMENT

In an experience covering a considerable number of cases I have been impressed with the fact that it is difficult if not impossible to prognosticate the outcome in any 1 case. Irrespective of the plan of therapy employed, frequent examination of the larynx is imperative because of the rapid recurrence of simple keratosis in some patients and changes in others that suggest the occurrence of carcinoma. In certain cases, the patients recover on a regimen of no smoking, vocal rest, vitamin therapy and the removal of keratotic material by the use of cupped forceps or other appropriate means. In another group these therapeutic measures appear inadequate, and masses of keratosis reappear in spite of frequent removals without, however, any histologic evidence of carcinoma. In such cases it may be necessary to strip the vocal cords of their mucosal and submucosal coverings as described by Loré [11] and Putney and Clerf.[12] In a third group the clinical and histologic appearances are so suggestive of carcinoma that laryngofissure appears to be indicated, although study of the material removed at operation may fail to reveal any evidence of carcinoma; and, lastly, there is the group in which at some time or other during the course of the disease carcinoma develops in or about the site of the keratosis. Cases illustrating these groups will be cited.

REPORT OF CASES

Cases That Responded to Conservative Therapeutic Measures

A man aged 52 was observed eleven weeks after the onset of hoarseness, subsequent to an acute infection of the upper respiratory tract. He was a moderate smoker of cigarets. Mirror laryngoscopy revealed extensive keratosis which involved the upper surface and edge of the right vocal cord. Direct laryngoscopic removal of keratotic areas was performed and all the material was examined histologically. This revealed hyperplastic epithelium with moderate inflammatory changes in the submucosa. There was no evidence of carcinoma (fig. 3). The patient was placed on a regimen of no smoking and moderate use of his voice and given large doses of combined vitamins. A second laryngoscopy was necessary to remove additional keratotic material. The patient made a satisfactory recovery, and there has been no recurrence of keratosis for over eight months.

Cases Requiring Frequent Removal of Mucosal and Submucosal Tissues

A man aged 48 was first examined in September 1941. He had been hoarse for one year after a cold. He was an excessive smoker of cigarets and used alcohol moderately. Mirror laryngoscopy revealed a whitish granular-appearing lesion on the upper surface of the anterior half of each vocal cord. Both cords exhibited definite inflammatory changes and the edges appeared irregular, suggestive of probable neoplastic changes. Biopsies were performed from both cords. There was pronounced hyperplasia of epithelium with inflammatory infiltration of the submucosa (fig. 2). The patient was advised to discontinue smoking and placed on combined vitamin therapy but failed to cooperate. A total of fourteen removals of keratotic material were performed over a period of four and a half years, and all the tissue was examined histologically. On five occasions the pathologist reported that the changes were extremely suggestive of early carcinoma, but no positive diagnosis could be made. In February 1944, two and one-half years after treatment was begun, the left cord remained free of keratosis, and when the patient was last seen in April 1946 there still appeared a small patch on the right vocal cord. At no time after the first examination did the clinical appearances suggest carcinoma, and for that reason it was decided not to carry out any radical surgical procedure, for the extent was such that both vocal cords would have had to be removed. The patient now is following the prescribed plan of therapy, and the prognosis appears good.

Cases Not Frankly Carcinoma but Requiring More Radical Therapeutic Measures

This group is represented by 2 men, aged 48 and 67 respectively, who had unilateral keratosis involving the anterior half of the right vocal cord. The lesions appeared nodular with decided inflammatory changes and were suggestive of carcinoma. The biopsy report was keratosis with many mitotic figures and pronounced submucosal inflammation. Although a positive histologic diagnosis of carcinoma could not be made, the lesions nevertheless appeared clinically to be suggestive of carcinoma, and for that reason laryngofissure was performed. The membranous vocal cord was removed in each case and studied histologically, but in neither case was there evidence of carcinoma. These patients developed excellent voices, since

11. Loré, J. M.: Stripping of the Vocal Cords, Arch. Otolaryng. **42**: 378 (Nov.-Dec.) 1945.
12. Putney, F. J., and Clerf, L. H.: Treatment of Chronic Hypertrophic Laryngitis, Arch. Otolaryng. **31**: 925 (June) 1940.

removal of the cord did not include the perichondrium, and a satisfactory vocal band ultimately developed.

Cases of Keratosis Which Ultimately Exhibited Histologic Evidences of Carcinoma

This group consisted of 4 cases in which the patient's disease had been under treatment for prolonged periods as keratosis but ultimately developed into carcinoma. In 3 cases laryngofissure was performed and in 1, a laryngectomy.

CASE 1.—A man aged 55 was first observed in February 1938. There was a history of keratosis with hoarseness of two years' duration. At the time of observation in 1938, there was an area of keratosis on the upper surface of the right vocal cord, anteriorly, with a larger patch on the upper surface of the left vocal cord, involving its middle and anterior thirds. The histologic report was hyperplasia and keratosis of the epithelium with submucosal inflammation. There was no evidence of carcinoma. The patient returned to his physician, a laryngologist, who kept him under observation, and no change was observed until the fall of 1942, three and one-half years later, when a papillary lesion appeared on the left vocal cord. Biopsy revealed a squamous cell carcinoma. The lesion was

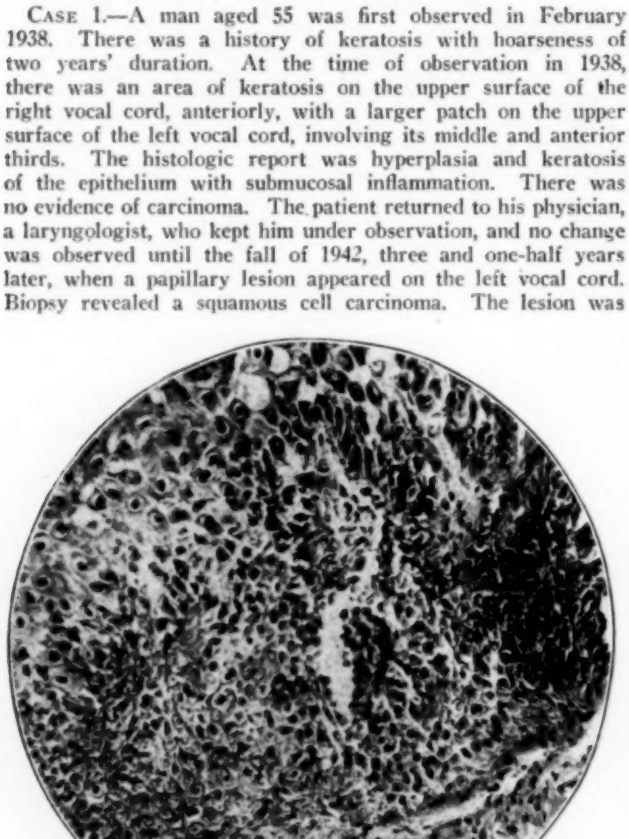

Fig. 4.—Photomicrograph (× 200) revealed definite epithelial hyperplasia, deeply staining nuclei and occasional mitosis. The basement membrane was only fairly well defined. There was considerable submucosal inflammation. Over three years later a small area of carcinoma was discovered by biopsy.

small and was removed by laryngofissure in November 1942. The patient has had no recurrence of carcinoma or keratosis since that time.

CASE 2.—A man aged 53 was first observed in August 1943. He was an excessive smoker of cigarets. A diagnosis of chronic laryngitis had been made over two years previously, and he was kept under observation. When he was examined in 1943, there was a white lesion with small villous projections on the anterior half of the right vocal cord. A histologic diagnosis of keratosis was made. There was no evidence of submucosal invasion. There were many mitotic figures, and there was submucosal infiltration with round cells. Dr. Bucher who examined the tissue stated that while the histologic appearances were those of keratosis the extent of involvement and the associated submucosal inflammatory changes together with the occurrence of mitotic figures suggested that this was a borderline case (fig. 4). The patient discontinued smoking and was placed on vocal rest. In April 1946, over three years later, there was an increase in hoarseness, and a granular nodule was found on the right vocal cord in its anterior third. The biopsy report was squamous cell carcinoma, intermediate grade. The lesion was removed by laryngofissure.

CASE 3.—A man aged 38, an inveterate cigaret smoker, had been hoarse for eight months. On examination in October 1942 there was observed keratosis on the upper surface and edge of each vocal cord, anteriorly, extending into the anterior commissure. There was definite heaping up of keratotic material on the right cord suggestive of a nodule. A biopsy revealed no carcinoma. The epithelium was thickened, but there was little submucosal inflammation. Five removals of keratotic material from both vocal cords were performed during the succeeding eight months. All the tissue was negative for carcinoma. For a time there was no recurrence of keratotic material, but in January 1944 there was a recurrence of a large mass on the upper surface of the left vocal cord and of a smaller mass on the right cord. Biopsy of the left cord revealed carcinoma. A laryngofissure was performed and both vocal cords were removed.

CASE 4.—A man aged 46 was first examined in August 1943. He had been under observation and treatment elsewhere for three years. Various diagnoses had been made, including keratosis, fungus infection and carcinoma. He had been given large quantities of vitamin A with some resultant improvement in the voice but no apparent change in the larynx. On examination a large granular white area was observed on the edge and upper surface of the right cord. The left cord was normal. The appearances were suggestive of carcinoma, but a biopsy was negative. Additional tissue was removed with negative findings. Because of the apparent lack of improvement and the duration of symptoms for more than five years the patient changed physicians, and the larynx was not examined for one year. He returned in May of 1946 with an extensive ulcerated lesion involving the entire right vocal cord. A biopsy revealed a squamous cell carcinoma, and it was necessary to perform a laryngectomy.

COMMENT

While keratosis is often observed in association with carcinoma of the larynx, the 4 cases cited herein exhibited evidences of keratosis of the larynx for two to four and one-half years from the time that I first observed them until a diagnosis of carcinoma was made; and, in addition, it was known that keratosis was present for eight months in 1 case, two years in 2, and three years in 1 case before the patients were examined by me. It is evident therefore that I was dealing with keratosis in the beginning and that carcinoma developed later. While there is no evidence to indicate that the keratotic cells ultimately assumed a malignant character, there is justification for the statement that patients with keratosis of the larynx should be carefully observed because in a certain proportion of cases carcinoma will develop.

CONCLUSIONS

Keratosis of the larynx is a relatively common benign condition. It is more often observed in adult males and particularly in those who smoke excessively.

There is experimental and clinical evidence to suggest that keratosis of the larynx is a manifestation of a metabolic or a food deficiency disease.

Clinical observations indicate that although keratosis per se is benign, there are a certain number of keratoses that either become carcinoma or predispose to its development.

While the outstanding changes observed histologically in these cases are epithelial hyperplasia and submucosal inflammation, it is impossible for the pathologist to anticipate in any given case that cancer will develop, although at times it is difficult to differentiate between early carcinoma and simple keratosis.

Patients with keratosis of the larynx should be kept under close observation; the involved areas should be removed and all tissue examined histologically. If there is any question of the occurrence of carcinoma, more radical surgical intervention is indicated.

VENOUS THROMBOSIS

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The significance of venous thrombosis is exemplified by the interest which is shown in this subject by physicians in general. The fact that on the present program of the Section on Surgery, General and Abdominal, of the American Medical Association three titles are concerned with the subject of venous thrombosis is indicative of the importance of the condition. The significance of venous thrombosis is further demonstrated by the observations in McCartney's [1] autopsy cases. In 25,771 necropsies performed at the University of Minnesota from Jan. 1, 1919 to Dec. 31, 1938, death was due to pulmonary embolism in 687 (2.67 per cent). Even more remarkable was the disclosure that in 107 of the cases embolism had already occurred, or a thrombus existed which could have produced a fatal embolism. Venous clotting is of importance not only because of the symptoms which are associated with certain types, but also because of the possible sequelae, such as the persistence of symptoms subsequent to thrombophlebitis or even the occurrence of death from pulmonary embolism.

Clinical experience and experimental observations have resulted in a conviction that one cannot consider all venous thromboses as the same type of lesion, but that one must differentiate between two types which are different etiologically, symptomatically, prognostically and therapeutically. Unless there is a differentiation between these two types of venous thrombosis, the therapy is likely to continue to be unsatisfactory. In 1939 DeBakey and I [2] emphasized the importance of differentiating thrombosis associated with an inflammatory process of the vein from that of the bland thrombus occurring in a vein in which there is no inflammatory lesion. At that time the suggestion was made that in addition to considering thrombophlebitis, which designated that condition in which there is an inflammatory process involving the vein associated with thrombosis, the physician must consider phlebothrombosis, which "may be defined as partial or complete venous occlusion by an intravascular clot which is unassociated with inflammation, the clot being loosely attached to the vein wall." This differentiation has been emphasized in subsequent publications [3] and has been generally accepted, although there are a few who have not been willing to accept the designation of phlebothrombosis or to admit that such a condition occurs, maintaining that in all instances an underlying inflammatory process is responsible for the development of thrombosis in the patient. Jensen [4] expressed the opinion that phlebothrombosis does not occur except after trauma and will occur only in incised, lacerated or abraded wounds. On the other hand, Hunter and his associates [5] expressed the opinion that phlebothrombosis and thrombophlebitis are two distinct entities. Their conclusion was based on a careful anatomic investigation and was not a mere clinical presumption, which is apt to be inaccurate. In 350 unselected autopsies, the veins of the calf muscles were examined in 209 instances. Venous thrombosis was found in 185 cases, and in only 17 instances (9.1 per cent) was there evidence of a phlebitis; in the remainder there was no evidence of an inflammatory process, although a thrombus was present in the veins. These authors concluded that as far as thrombosis of the veins of the calf muscles is concerned, inflammation of the vein, i. e. phlebitis, has little to do with the production of the clot.

The mechanism of the clot formation in the two types of venous thrombosis, thrombophlebitis and phlebothrombosis, is entirely different. In thrombophlebitis, as a result of the inflammatory process of the vein wall, there are changes within the vascular endothelium which predispose to clotting. This is similar to the process that occurs when a sclerosing agent is introduced into a varicosity. In the spontaneously occurring thrombophlebitis, the inflammatory process is usually the result of involvement of the vein secondary to perivenous lymphangitis, the micro-organisms being carried to the vein through the lymphatic system. In some instances there is evidence that the changes in the vascular endothelium are not due to bacterial invasion but may be caused by toxins or allergic sensitization (Turnbull [6]). In thrombophlebitis, unless it is associated with a severe suppurative process such as lateral sinus thrombophlebitis or portal thrombophlebitis, the femoral and iliac veins are usually the ones involved. Since the thrombus in thrombophlebitis is the result of inflammatory change in the vein wall, particularly the endothelium, the resultant clot is either a white or a mixed thrombus and is firmly attached to the vein wall. For this reason, with two possible exceptions, thrombophlebitis is not associated with embolism because the clot is attached and cannot become detached. The first of the two exceptions is the possible formation proximal to the area of thrombophlebitis of a bland thrombus, or coagulation thrombus, which is not attached and which can become detached. This is usually of little significance, because it is a relatively short clot, and if it did become detached it would produce a small infarction. The formation of such a clot should not be permitted, and it can be prevented by mobilization of the involved extremity during the treatment of the thrombophlebitis. The other exception is suppurative thrombophlebitis in which, as a result of liberated proteolytic ferments, the fixed clot can become liquefied and permit fragments to break off with the resultant production of septic emboli. This is usually observed in patients with severe pelvic infections and is generally subsequent to criminal abortion. In this instance, the detachment of the thrombus is the result of a suppurative process and does not result because the clot was detached. In contrast, the mechanism of the formation of the thrombus in phlebothrombosis is entirely different. There is no inflammatory process

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Because of lack of space, this article is abbreviated in THE JOURNAL by omission of portions of the text and footnotes. The complete article will appear in the author's reprints.

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6. Turnbull, J. A.: Allergy as a Factor in Thrombosis, Am. J. Digest. Dis. **10**: 194, 1943.

in the vein wall, and the clot is the result of two factors, the increased coagulability of the blood and the slowing of the blood stream. The clot which is formed is a red or coagulation thrombus similar to the clot which occurs in a test tube when blood is withdrawn from the vascular system. It is only loosely attached to the vein wall; it can become detached relatively quickly, with the same ease as the coagulum which appears in the test tube can be detached from the walls of the tube when the tube is inverted. These thrombi, as has been shown repeatedly by autopsies,[8] usually originate in the veins of the calf muscles or in the veins on the plantar aspect of the foot but may extend up into the deep veins of the thigh and pelvis. They are extensive thrombi and, since they are not firmly attached, are of real potential danger, because of the possibility that they will be detached and carried through the venous system to the heart and lungs, thereby producing varying grades of infarction from relatively insignificant peripheral infarction to total occlusion of both pulmonary veins, with sudden death. It is possible, if for some fortunate reason the coagulation thrombus in phlebothrombosis does not become detached, that sufficient inflammatory reaction will occur in the intima of the vessel and firm attachment will ultimately take place. Bauer[9] expressed the belief that this process begins soon after the formation of the thrombus. I am of the opinion, however, that it is a late and infrequent phenomenon and should not be anticipated.

Although the mechanism for the development of the thrombus in thrombophlebitis is readily understandable, the mechanism for the development of the coagulation thrombus in phlebothrombosis is less obvious. In the former disease, as mentioned previously, the clot formation is dependent on changes within the wall of the vessel, particularly in the intima. In the latter, thrombosis is dependent on an increased coagulability of the blood, which results from changes in the blood's constituents, because of trauma. Shafiroff and his co-workers[10] showed that 92 per cent of the patients with postoperative venous thrombosis and primary acute thrombophlebitis had hypercoagulability of their blood, and that the average acceleration of blood coagulation in these patients was four and one-half times that in normal subjects. Localization of the clot in the veins of the lower extremity is dependent on the slowing of the blood stream in that part of the body. It is my belief, as well as that of others, that as a result of tissue injury, and with few exceptions, whatever the cause of the injury, changes in the blood's constituents occur which favor blood clotting. This is undoubtedly a protective mechanism and is responsible for the lack of persistent hemorrhage in severe trauma. As a result of operative trauma, trauma during delivery, accidental trauma and the injury of tissue by the invasion of neoplastic disease or infection there is an increased clotting tendency. Because of its manifold causes it is essential that the possibility of venous thrombosis, particularly phlebothrombosis, be considered in all patients who have suffered a trauma. The greater the trauma, the greater the tendency toward thrombosis.

Although the increased clotting tendency is the underlying and predisposing factor in phlebothrombosis, the precipitating factor is circulatory stasis, and it is this factor which is responsible for the development of the thrombi in the veins of the calf muscles and on the plantar aspect of the foot rather than in the veins of the upper extremity. In addition to these two factors, increasing age (probably because of the associated cardiovascular disturbance) and alterations of the vascular system are particularly likely to be associated with venous thrombosis. The presence of cardiac disease is especially important in the production of venous thrombosis. Hunter and his associates[5] found at autopsy that thrombosis of the deep veins of the leg in middle aged and old persons who had been in bed for varying periods of time was as high as 52.7 per cent. The involvement was bilateral in 110 instances and unilateral in 75 instances. Allen[18] stated that 82.3 per cent of his patients with venous thrombosis were above the age of 40. Veal and Hussey[19] found that 70 per cent of their 84 cases of venous thrombosis were in patients over 40 years of age.

There is a definite relationship between venous thrombosis and the seasons. This has been repeatedly emphasized.[3b, e] Allen, Linton and Donaldson[21] observed 32.9 per cent of their cases in the winter, 21.9 per cent in the spring, 18.9 per cent in the summer and 20.3 per cent in the fall in a series of 332 cases. It is my belief that the increased incidence of venous thrombosis during the winter months is due to the vasospastic influence of the cold weather. This explains the difference between the incidence of venous thrombosis observed in the northern and in the southern clinics. My associates and I[3e] showed that the incidence of venous thrombosis in the northern clinics was almost double that in the southern clinics. The average incidence in the northern states was 0.74 per hundred thousand population as contrasted with 0.41 in the southern states.

Other predisposing factors in this disease are obesity, debility, changes in the hemopoietic system, such as anemia and polycythemia, and excessive smoking.

As mentioned previously, increased coagulability resulting from changes in the blood's constituents because of tissue injury is one of the most important factors in the production of venous clotting, particularly phlebothrombosis. These changes in the blood are manifold, and the exact role played by each is not known, but probably all combine to exert a definite effect on the clotting mechanism.

In addition to the predisposing factors which favor blood clotting, the precipitating factors as mentioned previously are those which cause circulatory stasis. Any condition which produces a slowing of the blood stream is likely to result in the production of a coagulation thrombus in a person with an increased clotting tendency as a result of tissue damage. McCartney[1] pointed out that venous thrombosis occurred five to six times more frequently in cases which showed chronic passive congestion in the liver than in cases in which the liver was normal. The movement of blood in the

8. (*a*) Homans, J.: Venous Thrombosis in the Lower Limbs: Its Relationship to Pulmonary Embolism, Am. J. Surg. **38:** 316, 1937. Rössle, R.: Ueber die Bedeutung und Entstehung der Wadenvenenthrombosen, Virchows Arch. f. path. Anat. **300:** 180, 1937. Neumann, R.: Ursprungszentren und Entwicklungs formen der Bein-Thrombose, ibid. **301:** 708, 1938. (*b*) Hunter, W. C.; Krygrer, J. J.; Kennedy, J. C., and Sneeden, V. D.: Etiology and Prevention of Thrombosis of the Deep Leg Veins: A Study of Four Hundred Cases, Surgery **17:** 178, 1945. Hunter, Sneeden, Robertson and Snyder.[5]

9. Bauer, G.: Heparin Therapy in Acute Deep Venous Thrombosis, J. A. M. A. **131:** 196, (May 18) 1946.

10. Shafiroff, B. G. P.; Doubilet, H.; Barcham, I. S., and Co Tui: The Coagulability of Venous Blood of Normal and Diseased Legs: A Study of One Hundred Ninety-One Subjects, Ann. Surg. **118:** 482, 1943.

18. Allen, A.: Thrombosis and Embolism: A Preliminary Report on the Comparative Results of Femoral Vein Interruption and Dicumarol Therapy, Bull. New York Acad. Med. **22:** 169, 1946.

19. Veal, J. R., and Hussey, H. H.: Surgery of Deep Venous Thrombosis of the Lower Extremity, Surgery **17:** 218, 1945.

21. Allen, A.; Linton, R., and Donaldson, G. A.: Venous Thrombosis and Pulmonary Embolism: Further Experience with Thrombectomy and Femoral Vein Interruption, J. A. M. A. **128:** 397 (June 9) 1945.

venous system is dependent on a number of factors, such as the vis a tergo through the capillary bed, which varies according to the degree of vasodilatation or vasoconstriction and depends on cardiac function. Naide [28] expressed the opinion that patients with a high grade vascular tone are particularly likely to have venous thrombosis develop because of diminished blood flow. In a series of 17 cases, 16 patients had a high grade vascular tone. Smoking would be particularly detrimental to such patients. Another factor in favoring the movement of blood in the venous system is the negative pressure within the thorax, facilitating the flow of blood from the distal parts of the body. The third, and probably the most important, factor in the movement of blood in the venous system is the active contraction of the skeletal muscles. Prolonged rest in bed is an important factor in producing circulatory stasis, unless measures are instituted to obviate it. Although the patient who is in bed frequently moves his hands and arms, reaches to the bedside table, places his hands on his head or moves them to his face, he is likely, unless otherwise instructed, to keep his lower extremities perfectly motionless. This lack of muscular contraction is a great factor in producing retardation of the blood in the lower extremities. If the patient has been subjected to an abdominal operation or has had an injury of the abdominal cavity, he is less likely to breathe deeply because of the pain resulting from deep inspiration. This favors circulatory stasis, and as a result of a trauma, particularly of the abdomen, there is the likelihood of diminished circulation in the lower extremities because of vasospasm. If, in addition to these factors, there is increased intra-abdominal tension because of abdominal distention and the use of tight bandages, stasis within the veins of the lower extremities is greatly increased. The position which the patient assumes in bed is of importance. If he is placed in a head up position or particularly in a Fowler's position with the knees flexed on the thigh and the upper part of the body elevated, stasis in the calf veins is favored not only by gravity but also by the kinking of the popliteal veins in the popliteal space.

SYMPTOMATOLOGY

As mentioned previously, the differentiation between phlebothrombosis and thrombophlebitis must be made not only from an etiologic standpoint but also from that of clinical manifestations. In most cases of thrombophlebitis, the clinical picture is definite and well defined. The patient usually complains of pain in the involved extremity, there is usually a pyrexia, and with few exceptions there is swelling of the extremity. Color changes in the extremity are of significance. In cases with deep vein involvement (the type which is more common) there is a characteristic whiteness of the extremity, as suggested by the descriptive term "phlegmasia alba dolens." The temperature of the skin of the involved extremity is cool, which is an obvious paradox in view of the increased surface temperature of the rest of the body.

In superficial vein involvement the skin overlying the affected vein is red and warm. The fever is due to the inflammatory process in the involved extremity; the pain is due to an ischemia and is relieved by vasodilatation. The whiteness of the extremity, concerning which there has been considerable controversy in the past, is unquestionably due also to vasospasm, and this too is relieved by vasodilatation. The edema in thrombophlebitis was previously thought to be caused by increased venous pressure which resulted from the obstruction within the involved vein. The fact that a large vein such as the femoral, iliac or even vena cava can be ligated with the production of only transitory edema is certainly evidence against the hypothesis that the edema is due to obstruction of the vein. My associates and I [29] have previously shown that the edema is due to the ischemia resulting from arteriolar spasm and is promptly relieved by vasodilatation.

Although the patient with thrombophlebitis appears ill and is uncomfortable because of the pain, fever and swelling, the patient with phlebothrombosis is likely to have no symptoms whatever. In fact, I am convinced that the diagnosis must be made before any symptoms are manifest because usually the symptoms are the result of a complication, such as infarction or a beginning inflammatory process resulting from the retained thrombus. Although many of these patients complain of a sense of impending disaster (which should be considered of great significance in a patient who has had any tissue injury, because of the likelihood of an existing phlebothrombosis) they usually do not have fever. There may be an elevation of the pulse rate which is decidedly out of proportion to any elevation of temperature, because the latter, if present, is almost insignificant. An almost constant observation is an increased erythrocytic sedimentation rate. Because the patient with phlebothrombosis has few or no symptoms, the diagnosis must be made by careful routine examination of the lower extremities in all patients who have had any tissue damage. It is my rule routinely to palpate the calf muscles and the plantar aspect of the foot and to dorsiflex the foot forcefully (Homans' sign) in all patients who are in bed and who have had tissue injury. The detection of tenderness in the calf or on the plantar aspect of the foot, or the production of pain in the calf or popliteal space when the foot is forcefully dorsiflexed is indicative of phlebothrombosis. Although previously I thought that a suspected phlebothrombosis should be verified by phlebography, I now believe that phlebography is not necessary, and that immediate therapy should be instituted before the clot has a chance to become detached.

PROGNOSIS

The prognosis in thrombophlebitis and that in phlebothrombosis differs considerably in the untreated patient, although the prognosis need not be bad in either instance, if appropriate therapy is instituted early. The patient with thrombophlebitis, unless there is suppuration (in which event the thrombus may be liquefied with the detachment of small septic emboli) usually gets along well and does not succumb to the thrombotic process. The patient is likely to have postphlebitic symptoms which may last for many years. These consist of swelling, pain, possible ulceration and streptococcic infection in the involved extremity. The patient may be incapacitated for months, for years or

28. Naide, M.: A Test for Vascular Tone in Humans and Its Application to the Study of Vascular Diseases with Special Reference to the Etiology and Prevention of Thrombophlebitis, Am. J. M. Sc. **207**: 606, 1944.

29. (*a*) Ochsner, A., and DeBakey, M. E.: Thrombophlebitis: Role of Vasospasm in Production of Clinical Manifestations, J. A. M. A. **14**: 117 (Jan. 13) 1940. (*b*) DeBakey, M.; Burch, G. E., and Ochsner, A.: Effect of Chemical Irritation of Venous Segment on Peripheral Pulse Volume, Proc. Soc. Exper. Biol & Med. **41**: 585, 1939. (*c*) DeBakey, M.: The Role of Vasospasm in Thrombophlebitis and Its Treatment by Novocaine Block of the Sympathetics, Tri-State M. J. **13**: 2654, 1941. DeBakey, M., and Ochsner, A.: Novocaine Sympathetic Block Method of Therapy in Thrombophlebitis, J. M. A. Alabama **11**: 87, 1941. Ochsner, A., and DeBakey, M.: Symposium on Vascular Thrombosis: Rational Therapy of Thrombophlebitis, New Orleans M. & S. J. **94**: 173, 1941. Footnote 3 *b*, *c* and *e*.

for the rest of his life. On the other hand, the patient with phlebothrombosis is a potential fatality unless active measures are taken, because the thrombus is not firmly attached and can become detached on the slightest exertion. Although nonfatal infarction with a resulting pneumonitis can occur, the possibility of a massive pulmonary embolism resulting in sudden death is not only feasible but likely.

THERAPY

The initial treatment of venous thrombosis consists of prophylaxis. It is my belief that in most cases clotting within the venous system can be prevented if appropriate measures are instituted. Preoperatively, it is important that patients with cardiovascular disturbance should be treated to reestablish the cardiovascular function before a contemplated operative procedure is undertaken. This is particularly important in older persons and in patients with cardiovascular disease. I believe, too, that a patient who is to undergo an operative procedure should refrain from smoking for a period of from ten to fourteen days preoperatively because of the vasoconstrictor effect of smoking. Duryee [30] has emphasized the importance of this. Naide [28] showed that patients with increased vascular tone have a greater tendency to venous thrombosis. In order to increase the rate of blood flow through the deep veins it has been my practice, for many years, to apply compression bandages to the extremities in patients 40 years of age or older who are subjected to an operative procedure. No. 8 Ace bandages are applied to both lower extremities from the toes to the groin before the patient leaves the operating room. This is done not only in patients who have undergone an operation, but also in nonsurgical patients in whom there is destruction of tissue as a result of infection, neoplastic disease or trauma. The compression of the superficial veins by means of bandages increases the flow of blood through the deep veins and overcomes circulatory stasis. This is particularly advisable in the patient who has varicosities, because of the greater likelihood of the stasis of blood in the dilatated superficial veins.

Since obesity is a factor in predisposing to venous thrombosis, reduction of weight in the elective surgical case is of importance before the operative procedure is attempted. Also, the correction of any blood dyscrasia, such as anemia or polycythemia, is extremely desirable as a prophylactic measure.

Since the increased coagulability of blood is dependent on tissue injury, it is imperative during an operative procedure to avoid as much trauma as possible. The use of sharp dissection, the avoidance of mass ligation and the use of fine nonabsorbable suture material (particularly cotton, because it produces a minimal amount of wound reaction) decrease the tendency toward clotting. The prevention of circulatory collapse during the operation and the immediate postoperative period by the administration of fluids, and particularly by the reestablishment of blood volume, are of importance. Postoperatively, the avoidance of abdominal distention by means of the indwelling duodenal or double catheter along with the avoidance of tight abdominal bandages will decrease the pressure exerted on the abdominal veins which, in turn, will tend to obviate the stasis of blood in the lower extremity. A patient who has recently been operated on should be placed in the head down position immediately on return to his room, because in this position gravity favors the return of venous blood from the lower extremities. This position should be maintained until the patient has recovered sufficiently to contract actively the muscles of his leg and thigh. The head up position, particularly Fowler's position (the patient in the sitting position with the legs flexed on the thighs) must be avoided for the reasons which have already been given. As soon as the patient can do so, active muscular contraction of the calf muscles against a resistance is imperative. I insist on forceful ventroflexion of the foot against resistance many times during the day. In order to increase the return venous flow deep breathing is essential; by increasing the negative pressure within the thorax, the blood flow into the thoracic veins is favored.

Early ambulation of the patient is of importance in decreasing the incidence of venous thrombosis, but simply getting the patient out of bed is not sufficient to protect against venous clotting. In fact, many instances of so-called ambulation actually do more harm than good. Certainly, to allow a patient to sit in a chair with his legs dependent produces greater circulatory stasis in the veins of the lower extremity than that produced if he contracts his musculature actively against a resistance while lying in the horizontal position. If by ambulation it is meant that the patient walks, this will undoubtedly decrease the incidence of venous thrombosis.

Although theoretically the administration of anticoagulants to all patients who were operated on might be of value, I believe that their use is too dangerous to be invoked routinely. In the person who has had previous thromboses and who probably has a thrombosing tendency, heparin or Dicumarol (3,3'-methylene-bis-[4-hydroxycoumarin]) prophylactically might be used immediately after operation. In this way, the possibility of thrombosis could be avoided. In fact, it is my feeling that the use of anticoagulants should be limited largely to patients in this classification. Allen [21] used Dicumarol prophylactically in a series of 101 cases in patients between the ages of 40 and 65. In 3 patients venous thrombosis developed and in 6 there was some hemorrhage which may or may not have been due to the anticoagulant. De Takats [32] has warned that if anticoagulants are used in conjunction with sulfonamides great caution should be exercised, because sulfonamides increase the heparin sensitivity. Similar caution is necessary when anticoagulants are used with neostigmine—de Takats and Fowler [33] Reich and others [34] have also used anticoagulants prophylactically with good results.

ACTIVE THERAPY

The active treatment of venous thrombosis, once the thrombus has occurred, differs according to the type of thrombosis; and the urgency also varies according to the type. In thrombophlebitis in which, as has been mentioned, there is fever, pain and swelling of the extremity, the treatment consists of vasodilatation secured by procaine hydrochloride block of the regional sympathetic ganglions since the symptoms in thrombophlebitis are due to vasospasm. It has been shown both clinically and experimentally that although the

30. Duryee, A. W.: Thrombophlebitis: Medical Treatment, Bull. New York Acad. Med. **20**: 604, 1944.

32. de Takats, G.: The Effect of Sulfa Compounds on Blood Clotting, Surgery **14**: 661, 1943.

33. de Takats, G., and Fowler, E. F.: The Problem of Thrombo-Embolism, Surgery **17**: 153, 1945.

34. Reich, C.; Yahr, M. D.; Eggus, C., and Lipkin, D.: Dicumarol in the Prevention of Postoperative Thrombosis and Pulmonary Embolism, Surgery **18**: 238, 1945.

lesion in thrombophlebitis is limited to one of the major veins, the symptoms are dependent on associated arteriolar spasm, and that by relieving the spasm, the symptoms quickly subside. The pain is relieved instantly, the temperature falls rapidly and the swelling subsides within a few days. There is a dramatic response to procaine hydrochloride block of the regional sympathetic ganglions in an ill patient who is extremely uncomfortable; the patient is not only relieved of his symptoms but is also spared such persistent manifestations as postphlebitic edema, pain, ulceration and recurrent streptococcic infection. My experience has shown that the relief of pain is complete and permanent in 90 per cent of the patients, whereas in 10 per cent a second block is necessary to give permanent relief. Sixty-five per cent of the patients treated with procaine hydrochloride anesthetization of the regional sympathetic ganglions were fever free within forty-eight hours after the institution of therapy, 24 per cent in three to five days and 7 per cent in six to eight days. In only 4 per cent did the pyrexia last longer than eight days. The edema completely subsided within four days or less in 56 per cent, in from five to eight days in 32 per cent, in from nine to ten days in 8 per cent, and in from eleven to twelve days in 3 per cent. Sixty-two per cent of the patients were discharged from the hospital as cured within four to eight days after the institution of therapy, 19 per cent left the hospital between the ninth and twelfth days and only 10 per cent remained in the hospital after twelve days. Similar results have been reported by many.[36]

The technic of the sympathetic block of the lumbar ganglions has been described repeatedly.[37] The injection of the first, second, third, and fourth lumbar ganglions, using 5 cc. of 1 per cent procaine hydrochloride into the region of each ganglion gives a satisfactory result. The injection should be performed every twenty-four hours as long as the patient has fever, because fever is an indication of the persistence of the inflammatory process. Although the pharmacologic effect of the drug persists much less than twenty-four hours, it is a well known fact that the physiologic effect of the injection of procaine hydrochloride into the sympathetic nerves lasts considerably longer than the pharmacologic effect.

In all uncomplicated cases of thrombophlebitis or phlegmasia alba dolens, conservative therapy is sufficient and, as exemplified by the results previously given, these patients are well within a short period of time. In the relatively rare case of suppurative thrombophlebitis, which is usually associated with a pelvic inflammatory disease resulting from criminal abortion in which there is liquefaction of the clot with the production of septic emboli, active radical therapy is imperative. Unless the involved vessel proximal to the site of involvement is ligated, septic infarction will continue, resulting in a fatality because of an overwhelming sepsis. In the past there has been considerable controversy among gynecologists concerning the advisability of venous ligation in these instances. The mortality rate has been extremely high because of their ultraconservatism. Miller [40] in 1917 collected 197 cases of puerperal pyemia treated by venous ligation with a gross mortality of 51.6 per cent. Unfortunately, at that time ligation was performed only as a last resort and usually when septicemia was already present. Since then the procedure has been used in many cases, although it has not become popular until recently. Dr. Conrad Collins [36b] of the gynecologic division has shown that the mortality rate in puerperal sepsis after criminal abortion can be greatly decreased by the early ligation of the vena cava and the two ovarian veins. If good results are to be obtained, the operation must be performed early, before sepsis has developed. Twenty-two patients with suppurative pelvic thrombophlebitis have been operated on by the gynecologic staff at Tulane University under the direction of Collins. Of these 22, 20 survived the procedure. One of the 2 fatalities was moribund when operated on and did not survive the operation. The other was admitted to the hospital late in the course of her disease and at the time of operation had extensive pulmonary suppuration. She succumbed six days later to suppurative disease of the lungs. These statistics demonstrate the advantage of radical therapy in suppurative thrombophlebitis and show that the previously accepted extremely poor prognosis in these cases is no longer necessary. Although there is some difference of opinion concerning the method of approach in ligating the pelvic veins in suppurative thrombophlebitis, I am convinced from my experience that transperitoneal ligation of the vena cava just above the bifurcation, together with ligation of the two ovarians, is the preferable method of approach.

With the exception of a suppurative process, the treatment of thrombophlebitis is that of conservatism. On the other hand, the treatment of phlebothrombosis in which the thrombus is not intimately attached to the vein wall and can be readily detached on the slightest exertion, is radical operative therapy in order to prevent the detached thrombus from being carried in the systemic venous system into the heart of the lungs. Although there are many (Barker [40a] and others [41] who believe that all forms of venous thrombosis can be treated by means of anticoagulants, it is my firm conviction that the use of anticoagulants alone in phlebothrombosis is hazardous, because, although the administration of anticoagulants will prevent the formation of additional thrombi, it will certainly not prevent the detachment of those thrombi which are already present. I cannot agree with Barker and his associates [40a] that when a thrombus is diagnosed clinically there is no danger that it may become detached and an embolus may form. As I mentioned before in discussing the symptomatology in phlebothrombosis, I believe that a coagulation thrombus can be detected by careful physical examination. Of course, if one waits until the clot becomes detached and produces pulmonary infarction or if the patient is fortunate enough that the thrombus

36. (*a*) Leriche, R., and Kunlin, J.: Tratamiento inmediato de la flebitis postoperatorias por la infiltración novocainica del simpático lumbar, Crón. méd. mex. **33:** 389, 1934. Leriche, R.: Traitement chirurgical des suites éloignées des phlébites et des grands oedèmes non médicaux des membres inférieurs, Bull. et mém. Soc. nat. de chir. **53:** 187, 1927. McPheeters, H. O., and Alexander, H. A.: Lumbar Sympathetic Block and That Postphlebitic Leg, Minnesota Med. **29:** 43, 1946. Nicholson, M. J.: Treatment of Thrombophlebitis by Paravertebral Block, S. Clin. North America **24:** 538, 1944. Aycock, T. B., and Hendrick, J. W.: The Problem of Venous Thrombosis, to be published. (*b*) Collins, C. G., and Nelson, E. W.: Phlebothrombosis and Thrombophlebitis in Gynecology and Obstetrics, paper read before the meeting of the American Gynecological Society, 1946.

37. Ochsner and DeBakey.[34] Footnotes 29 *a* and *c*.

40. Miller, C. J.: Ligation or Excision of the Pelvic Veins in the Treatment of Puerperal Pyemia, Surg., Gynec. & Obst. **25:** 431, 1917.

40a. Barker, N. W.; Cromer, H. E.; Hurn, M., and Waugh, J. M.: The Use of Dicumarol in the Prevention of Postoperative Thrombosis and Embolism with Special Reference to Dosage and Safe Administration, Surgery **17:** 207, 1945.

41. Crafoord, C., and Jorpes, E.: Heparin as a Prophylactic Against Thrombosis, J. A. M. A. **116:** 2831 (June 28) 1941. Murray, G. D. W.: Heparin in Surgical Treatment of Blood Vessels, Arch. Surg. **40:** 307 (Feb.) 1940. Evans, J. A.: Anti-Coagulant Therapy of Postoperative Venous Thrombosis and Pulmonary Embolism, S. Clin. North America **24:** 534, 1944. Townshend, W. H., Jr., and Honigman, A. H.: Clinical Use of Dicumarol, with an Analysis of Forty Cases, Bull. School Med. Univ. Maryland **29:** 61, 1944. Yahr, M. D.; Reich, C., and Eggers, C.: The Treatment of Thrombophlebitis, Surg., Gynec. & Obst. **80:** 615, 1945. Zucker, H. D.: Clinical Experiences with Dicumarol, J. A. M. A. **124:** 217 (Jan. 22) 1944, de Takats, Trump and Gilbert.[6] Duryee.[30] Reich, Yahr, Eggers and Lipkin.[34]

does not become detached until sufficient inflammatory reaction is formed in the vein to bring on a superimposed phlebitis, the diagnosis can be made without the careful examination. The observation of Hunter and his associates [5] that in 92 per cent of 209 autopsies in which thrombosis of the leg veins was found there was no evidence of phlebitis, is demonstrable proof that a bland thrombus can occur; and since it is not associated with evidence of inflammatory change, it is not fixed to the vein wall. I have repeatedly seen patients who have been treated with anticoagulants over varying periods of time, one for as long as five weeks, in whom there continued to be discharges of emboli which, fortunately, in most instances were not fatal. As mentioned previously, although the administration of anticoagulants will prevent the formation of new thrombi, it will in no way prevent the detachment of those thrombi which are already in existence; a false sense of security in the belief that everything possible is being done by the administration of anticoagulants is likely to lull one into a belief that the patient is in no danger.

Because the thrombus in phlebothrombosis is only loosely attached to the vein wall and can be detached by any slight exertion, it is my belief that immediate surgical intervention should be undertaken as soon as the diagnosis of phlebothrombosis is made. In fact, this condition takes precedence, as far as urgency is concerned, over any other case on the service except that of massive hemorrhage. I have known 2 instances in which a diagnosis of phlebothrombosis was made, but in which the operation was delayed until morning at the time of the regular surgical schedule. In both instances a fatal embolism occurred during the night, before the contemplated procedure was performed. Had the operation been performed at the time the diagnosis was made, these fatalities could have been averted.

Because the administration of anticoagulants will not prevent the detachment of clots (in fact, I know of nothing that will prevent the detachment of the clot), it is my belief that either ligation of the vein above the thrombus or opening the vein and aspirating the thrombus proximal to the opening with ligation below that site is imperative. This should be done bilaterally, because there is bilateral involvement in such a high percentage of the cases. Arthur Allen [21] and his associates at the Massachusetts General Hospital have had the greatest amount of experience with curative and prophylactic ligation for venous thrombosis. In a recent publication he stated that from 1937 to Oct. 1, 1945 1,468 veins were ligated in 816 patients. In this series bilateral ligation has become the method of choice. From 1937 to 1942, 280 veins were ligated in 202 patients; in 39 per cent the venous interruption was bilateral. In 1943, 299 ligations were performed in 165 patients, with 81 per cent bilateral; in 1944, there were 554 ligations in 280 patients, with 97 per cent bilateral, and in 1945, in 169 patients, 335 ligations were performed, of which 98.2 per cent were bilateral. The indications for ligation in the entire group were as follows: signs and symptoms of venous thrombosis in the leg veins, 47.37 per cent; signs of pulmonary infarction, 34.4 per cent, and prophylactic ligation in older persons likely to develop thrombosis, 18.3 per cent. The incidence of prophylactic ligation has increased from 9.2 per cent in 1943 to 25.7 per cent in 1944 and to 36.7 per cent in 1945. Whereas I agree heartily with the Boston group that venous ligation is imperative in phlebothrombosis I do not believe that ligation is necessary in thrombophlebitis except in the rare case of suppurative thrombophlebitis. The patient with nonsuppurative thrombophlebitis can be treated satisfactorily and expeditiously by vasodilation, and ligation in an instance in which the clot is firmly attached is unnecessary. However, to deny a patient with phlebothrombosis the advantage of the thrombectomy or ligation is hazardous because of the likelihood that detachment of the thrombus will produce nonfatal infarction or fatal embolism. Whereas femoral vein interruption is generally a fairly innocuous procedure, it probably should not be performed unless it is absolutely necessary.

The treatment of phlebothrombosis consists of exposure of the femoral vein in the upper end of Hunter's canal. This should be done under local anesthesia. The vein is exposed for approximately 6 cm. below the deep femoral and an incision made in the vein beneath the opening of the deep femoral. If there is free bleeding from the vein proximally, the superficial femoral distal to the profunda is ligated. If there is no free bleeding, a glass cannula is inserted proximally, with the maintenance of a mild suction as the cannula is introduced. In this way, the thrombus which extends proximally into the common femoral and possibly into the iliacs is aspirated. Aspiration is continued until there is free bleeding from the opening in the vein. Subsequent to this, the vein is ligated just above and below the opening. In most instances the involvement is limited to the femoral below the profunda. If, however, there is involvement of the profunda as well as the superficial femoral I believe that both the femoral and the profunda should be ligated. Homans [43] and Fine and Farr [44] have preferred ligation of the iliac to that of the femoral vein because they considered that there is less subsequent edema. Ingraham,[45] because of observations made on autopsy material, expressed his belief that femoral ligation is not sufficient in most cases, and little can be accomplished by it.

SUMMARY AND CONCLUSIONS

Venous thrombosis is a serious complication in both medical and surgical patients.

From the etiologic, pathologic, symptomatologic, prognostic and therapeutic point of view, it is necessary to differentiate between two types of venous thrombosis —thrombophlebitis and phlebothrombosis. Thrombophlebitic organic changes are found in the vessel wall as the result of perivenous lymphangitis produced by bacteria, toxins or an allergy. The thrombus which is the result of changes in the endothelium is firmly fixed to the vein wall. In phlebothrombosis the clot is the result of two major causes; a predisposing one which consists of increased blood coagulability as the result of tissue injury, and a precipitating one which is circulatory stasis. The thrombus is not firmly attached to the vein wall and can be detached easily.

The patient with thrombophlebitis has many manifestations, such as fever, pain, swelling and color changes in the extremity, whereas the patient with phlebothrombosis has few or no symptoms. The prognosis in thrombophlebitis as regards life is good; but unless adequate therapy is instituted postphlebitic sequelae such as edema, pain, ulceration and streptococcic infec-

43. Homans, J.: Deep Clot Venous Thrombosis in the Lower Limb: Preferred Levels for Interruption of Veins, Iliac Section or Ligation, Surg., Gynec. & Obst. **79**: 70, 1940.

44. Fine, J., and Farr, A.: The Surgical Therapy of Thrombosis of the Deep Veins of the Lower Extremities, Surgery **17**: 232, 1945.

45. Ingraham, E. S., Jr.: The Distribution of Thrombi in Veins of the Pelvis and Legs in Relation to the Possible Value of Ligation of the Femoral Vein, Canad. M. A. J. **47**: 553, 1942.

tion are likely. On the other hand, the patient with phlebothrombosis, although apparently not ill, is a potential fatality. The treatment of uncomplicated thrombophlebitis is conservative and consists of vasodilatation accomplished by anesthetizing the regional sympathetic ganglions. Only in rare cases of suppurative thrombophlebitis is radical therapy necessary; this consists of venous ligation proximal to the site of suppurative thrombophlebitis.

Phlebothrombosis, because of the great likelihood that the clot will become detached and produce pulmonary infarction or massive occlusion of the pulmonary artery which will cause sudden death, should be treated without delay by means of venous ligation or thrombectomy. Anticoagulant therapy may be used prophylactically in persons known to have a thrombosing tendency; however, in the treatment of phlebothrombosis it will prevent the formation of additional thrombi but will not prevent the detachment of the thrombus which already exists.

EFFECT OF SEASON AND DUST CONTROL ON COCCIDIOIDOMYCOSIS

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A complete description of the activities of the Commission on Epidemiological Survey of the Board for the Investigation of Epidemic Diseases, Preventive Medicine Service, will be presented in the Surgeon General's History of World War II. It may be mentioned here that a general consultative service was provided, together with standardized coccidioidin and facilities for serologic tests and Coccidioides identification. In conjunction with the Army Air Forces, a detailed epidemiologic investigation was carried out in four army air fields in the San Joaquin Valley, California (fig. 1). These investigations began in July 1941 at Minter and Gardner fields in Kern County, in February 1942 at Merced Army Air Field in Merced County and in March 1942 at Lemoore Army Air Field in Kings County. They continued until three of the fields closed, Gardner in March 1945, Lemoore in October 1945 and Minter in February 1946. On July 1, 1945, when Merced was transferred from the Training Command, the Merced study terminated because it had been shown that coccidioidomycosis was no problem there. Actually, Merced served as an unexpected "control."

The intensive epidemiologic investigations were based on coccidioidin testing permanent personnel and at first annually, later semiannually, retesting the negative persons. When the study began, it was not known whether the coccidioidin reactors were also immune, but it was soon apparent that those who reacted did not undergo clinical infections. This immunity was seen both in those who were infected while on the fields and in those who were found to be positive on arrival at the fields. The permanence of immunity will be discussed in a subsequent paper. Likewise, the relatively long duration of coccidioidin sensitivity, comparable to that of tuberculin, will be presented subsequently. When the personnel previously negative were retested, it also became evident that the proportion of completely inapparent or asymptomatic coccidioidal infections was larger than that of clinically recognizable disease.

At approximately monthly intervals permanent personnel who arrived subsequent to the previous visit were coccidioidin tested. Freshly [1] diluted 1:100 lot 9 coccidioidin was used throughout the study as a 0.1 millimeter intradermal test. While our other coccidioidins have been standardized against this lot 9, it was felt that using one lot would avoid any question of difference of antigen at the time of the retest. Except for brief periods [2] and at the retest, one person gave the tests and interpreted the results. At the retests, sometimes another of the investigators would test or interpret. However, the permanent tester was working alongside, and the same technics and interpretations were employed. If there was a question, the opinion of the permanent tester was obtained.

Records were kept of all those tested. If clinical coccidioidomycosis occurred, notation was made. At the retest, all who previously failed to react, except those who were known to have had a clinical coccidioidal illness, again were tested. The newly revealed reactors ("change overs") were interrogated regarding illnesses, additional epidemiologic information was obtained, blood for erythrocyte sedimentation rates and coccidioidal serology was drawn and, if possible, pulmonary roentgenograms were taken. The army form 52 A infirmary records and the hospital histories were also checked for suspicious illnesses. Eliminating those originally tested but no longer present at the retest, we grouped the retested persons into the uninfected

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From the Commission on Epidemiological Survey, Board for the Investigation of Epidemic Diseases, Preventive Medicine Service, Office of the Surgeon General. The special studies of coccidioidomycosis have been conducted in the Department of Preventive Medicine, Stanford University School of Medicine. The first five months of the study were supported by a grant from the Rosenberg Foundation. This has been a collaborative study. Dr. Francis G. Blake, chairman of the commission and president of the board, and Brig. Gen. S. Bayne-Jones, deputy chief of preventive medicine service, provided invaluable aid and counsel. In the Army Air Forces Brig. Gen. Charles R. Glenn while surgeon of the West Coast Training Center and the Training Command and ultimately as deputy air surgeon initiated and maintained Air Force cooperation. This was carried through by the surgeons of the Flying Training Command, Col. Otis B. Schreuder and Col. Michael G. Healy, and the deputy surgeon, Col. Bloyce H. Britton, by Col. Russel V. Lee, chief of professional services at Santa Ana army air base, and by Lt. Col. Norman Nixon, coccidioidomycosis control office of the Western Flying Training Command, by surgeons of the Fourth Air Force, Col. Fabian Pratt and Col. J. R. Copenhaver, and the executive officer, Lt. Col. P. M. Pederson,

(Footnote continued in next column)

and by the surgeons at the respective fields: Minter, Col. John Roberts, Col. A. L. Jennings, Lt. Col. E. C. Donohoe, Lt. Col. Benjamin Siebenthal, Lt. Col. Roger E. Weismann, Major Edward J. Hall and Major Maurice Foley; Gardner, Col. Robert R. Estill, Col. Albert Phillips and Major Robert G. McCurdy; Lemoore, Col. Edmund H. Padden, Col. D. D. Todorovic, Lt. Col. Harris D. Loe and Lt. Col. M. S. Wessell, and Merced, Col. M. U. Prescott, Col. Neill Johnson and Lt. Col. A. F. Dorner. The coccidioidomycosis control officers and chiefs of medicine contributed greatly to the study. Besides Major Homer G. Rosenberger, these Minter collaborators included Lt. Col. Russell W. Mapes, Lt. Col. Ian B. Hamilton, Major Maurice P. Foley and besides Capt. E. Gale Whiting at Lemoore, Lt. Col. J. Murray Kinsman and Lt. Col. Richard D. Evans. These collaborators at Gardner Field were Majors David H. Thurman and Clarence J. Keefe and at Merced, Majors Harvey A. Woods and Harry E. Thompson, Capt. David C. Whitehead. The roster of collaborating ward officers is too large to enumerate. Special mention should be given the hospital administrative officers who facilitated our work, particularly Chief Warrant Officer Melburn Biddulph at Minter. Key enlisted personnel who arranged for the scheduling and checking at tests included M/Sgt. Howard Sehlin at Minter, Pfc. (later Lieutenant) Wilbert M. Fitzpatrick and Sgt. C. O. Castledine at Gardner and Sgt. Robert A. Kunde at Merced. Many others assisted, including the various commandants, executive officers and Air Force commissioned and noncommissioned officer personnel. The post engineers, Major Daniel Eckerman of Minter, Capt. Clarence Church of Gardner and Capt. Robert H. Johnson of Lemoore, worked closely with us, as did Mr. H. J. Cremer and Major Howard B. Sprague, Army Air Force liaison officer, at the Ninth Service Command United States Army Engineers.

1. Studies have shown that if it is kept refrigerated and uncontaminated, coccidioidin in a 1:100 dilution retains its full potency over two years; at room temperature its potency is retained for well over six months.

2. During the five months from July to December 1941 Dr. E. E. Baker served as an associate in the testing at Minter and Gardner Fields, as did Dr. William Kirby during the period from February to April 1942 at Merced Field.

(still negative to coccidioidin) and the infected. The infected group included completely inapparent infections and clinically recognizable disease. The latter group included those patients whose histories showed either that their infections were not diagnosed when they were seen by the medical officers (missed cases) or that they did not report for medical care but "toughed it out" (atypical cases). To these undiagnosed cases in which the histories established that the patient had undergone clinical illness which could be allocated to a specific month of onset were added those clinically diagnosed cases still present at the retest.

Fig. 1.—Location of the four San Joaquin Valley, California army air fields which were the basis of the coccidioidomycosis study.

The first inquiry which invariably arises concerning coccidioidomycosis is the rate at which infection is acquired. The extremely rapid turnover of personnel made this calculation rather difficult. Of 1,200 nonreactors tested at Minter Field in July 1941, only 221 were present at retest one year later. We found that 52 had undergone infection, a rate of 24 per cent. Actually, this checked closely with 25.1 per cent calculated by the method to be described later. However, there were other years and other fields when the changes were even more drastic and additional calculations became necessary. Moreover, these calculations were imperative in estimating seasonal incidence.

The infection rates for the retested men were calculated as follows (table 1): The "inapparent infections" (column 3) were allocated to the months (column 1) according to the monthly percentage distribution of all clinically recognizable disease occurring in the field regardless of whether the former patients were still on the field (column 2). It was not possible to allocate

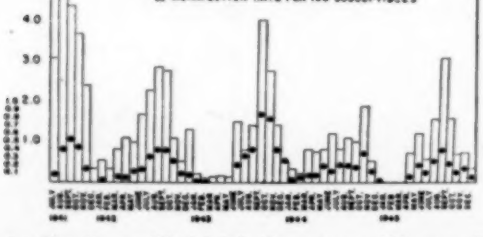

Fig. 2.—Monthly coccidioidal infection rate per 100 susceptible persons and monthly disease rate per 1,000 men at Minter Field, 1941 to 1945.

"inapparent infections" solely on the distribution of those still present who had clinically recognized disease since those still present were frequently so few that the fluctuation would have been like a tidal wave. The estimated "inapparent infections" (column 3) and the clinically recognizable infections present at the retest (column 4) were added to give the total number of infections per month (column 5). Newly tested negatives (column 6) were added to the residual negatives of the previous month (column 7, comprising column 8 minus column 5) to give the total number of those still negative and susceptible (column 8). The infection rate per 100 men (column 9) was calculated by dividing all infections (column 5) by total susceptibles (column 8). The monthly rates were then added to give the annual rate. It is to be observed that at Merced, where no clinically diagnosed infections were ever found to have been acquired on the field, it was impossible to calculate monthly infection rates. The annual infection rates were estimated by taking the number of coccidioidin negatives at the midpoint between the retests.

In table 2 are presented the monthly infection rates per 100 susceptible persons at Minter, Gardner and Lemoore together with the monthly precipitation in inches at the U. S. Department of Commerce Weather Station, Kern County Air Port, Bakersfield, Calif. For comparison the Minter Field monthly disease rate per 1,000 men field strength (total Army population on the field) is also given. The latter differs from the War Department records in that casuals were omitted and cases were allocated to month of onset rather than month when diagnosed. Figure 2 depicts the Minter Field infection rate per 100 susceptible persons and this monthly disease or case rate based on field strength. One notes the extremely poor monthly association. Indeed, the third coccidioidal season produced monthly disease rates higher than did the first, although calculated infection rates were significantly less. Figure 3 compares the monthly infection rates at Minter, Gardner and Lemoore, while figure 4 compares the monthly incidence at Minter Field with the monthly rainfall.

In table 2 the annual coccidioidal rates are presented for Minter, Gardner, Lemoore and Merced. Again one observes the inapplicability of the usual disease or case rate based on field strength. If one merely takes the average field strength for the year as a whole as the basis of computation, the results are even farther out of line. One fact is outstanding. Minter and Gardner, in the southern part of the San Joaquin Valley, have exceedingly high rates. In their first year with dust uncontrolled, 1 out of every 4 or 5 susceptible persons

TABLE 1.—*Example of Method of Calculating Monthly Coccidioidal Infection Rates, Minter Field, 1941 to 1942*

Inapparent Infections Distributed According to Monthly Incidence of Clinically Recognized Cases July 1941 to June 1942

Month	% Distribution of All Clinically Recognizable Cases*	Inapparent Infections	Clinically Recognizable Infections Present at Retest	All Infections	New Negatives	Previous Negatives Still Negative (8)—(5) of Previous Month	Total Susceptibles; (6)+(7)	Infection Rate per 100; (5)÷(8)
(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)	(9)
July	4.8	5	2	7	221	0	221	3.17
August	10.7	12	7	19	157	214	371	5.12
September	16.7	19	5	24	186	352	538	4.46
October	16.7	19	7	26	206	514	720	3.75
November	11.8	13	6	19	78	694	772	2.46
December	1.2	1	2	3	0	753	753	0.40
January	3.6	4	2	6	321	750	1,071	0.56
February	2.4	3	1	4	0	1,065	1,065	0.38
March	3.6	4	6	10	82	1,061	1,143	0.88
April	8.3	10	7	17	226	1,133	1,459	1.17
May	8.3	10	5	15	0	1,442	1,442	1.04
June	11.9	13	15	28	206	1,427	1,633	1.71
Total	100.0	113	65	178	1,783			25.10

* There were 84 clinically recognizable cases of coccidioidal infection.

was infected. Lemoore, 50 miles to the north, had half or less while Merced, another 75 miles north, had a negligible amount. Many of the "inapparent infections" detected at Merced were in men who had traveled into the southern part of the San Joaquin Valley. The Merced 1944-1945 calculations were complicated by the fact that at the time of the retest, Feb. 6, 1945, a considerable portion of the field personnel had migrated to Gila Bend, Ariz., because the land fogs in the San Joaquin Valley interfered with the training schedule. In the 728 previously negative persons who did not go to Gila Bend, the infection rate was only 0.5 per cent (essentially the same as in the previous two years). However, of 204 susceptible persons who went to Gila Bend January 6 to February 19, 4.8 per cent were found to be infected. Certainly the pattern of increased coccidioidal endemicity in the southern part of the San Joaquin Valley with a decrease as one proceeds northward is remarkably clear together with the implication of a high rate of incidence in Arizona.

The outstanding importance of dust in coccidioidomycosis is also apparent. Dust has been repeatedly [3] commented on as constituting the vehicle of "natural" infection. Coccidioidal chlamydospores are readily

TABLE 2.—*Annual Coccidioidal Rates in San Joaquin Valley Army Air Fields and Precipitation at Bakersfield, Calif., 1941 to 1945*

Year	Precipitation Previous Rainy Season	Minter (7/1 to 6/30) Disease Rate per 1,000 Men (Field Strength)	Minter (7/1 to 6/30) Infection Rate per 100 Susceptibles	Gardner (7/1 to 6/30) Infection Rate per 100 Susceptibles	Lemoore (3/1 to 2/28) Infection Rate per 100 Susceptibles	Merced (2/1 to 1/31) Infection Rate per 100 Susceptibles
1941-42	10.96	2.16	25.10	20.99		
1942-43	5.04	1.81	13.51	11.57	12.43	0.63
1943-44	9.64	3.89	15.61	13.58	6.21	0.36
1944-45	5.36	1.68	8.43	7.02*	2.86	1.4†
1945	7.36	1.34‡	8.35‡		1.43§	

* Gardner, July to November.
† Merced affected by Arizona exposures. See text.
‡ Minter, July to December.
§ Lemoore, March to September.

wafted in the air. The coccidioidal sporangia ("spherules") are infective when they are introduced into an animal's tissues.[4] However, they are much larger and do not constitute part of the infection chain unless, as Emmons hypothecates,[5] infected rodents die and their bodies furnish a medium in which the myceliums develop and infect the soil. Cattle,[6] sheep [6b] and dogs [7] as well as rodents and man are infected from the dust. When susceptible human beings stir up dust in highly infected areas, veritable epidemics occur.[3c,d] The seasonal characteristics of coccidioidal erythema nodosum ("valley fever") have been noted,[3b] but table 2 and figure 4 show this association with even greater clarity.

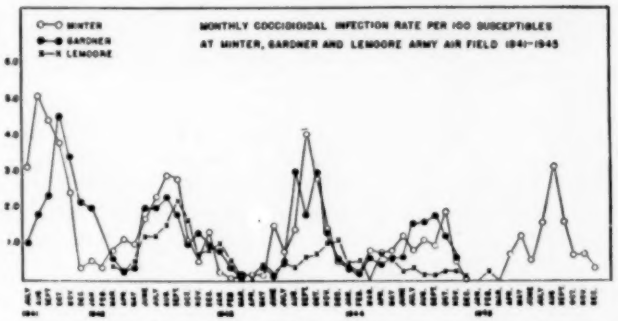

Fig. 3.—Monthly coccidioidal infection rate per 100 susceptible persons at Minter, Gardner and Lemoore army air fields, 1941 to 1945.

Recalling that the incubation period of coccidioidal infection is eight to twenty-one and possibly thirty days,[3b,c] one observes that the effect of rainfall is reflected not only in the month when the rain occurs but also in the succeeding month. The incidence is maximal in the dry summer and autumn, minimal during the winter and spring. The only exception in the data presented is in the Lemoore 1944 season (fig. 3). However, in June 1944 Lemoore changed from an active dust-raising training field to a much more sedentary processing center.

In the fall of 1941 when Minter and Gardner were being built there were extensive scarred surfaces and the dust billowed in clouds. That season of maximal dust provided the highest coccidioidal rates of the study (tables 2 and 3, figs. 2, 3 and 4). In the month of August 1941 over 5 per cent of the susceptible Minter Field personnel were infected.

The following year lawns were planted, roads were paved, air strips both at the main and auxiliary fields were hard-surfaced and the incidence of coccidioidal infections was cut in half. It may be noted (table 2) that the winter preceding the 1941 coccidioidal season had twice the rainfall of the succeeding winter, while the winter preceding the 1943-1944 season was another rainy one (for the San Joaquin Valley). There was an increase in coccidioidal incidence at both Minter and Gardner, suggesting that a wet winter season may aid

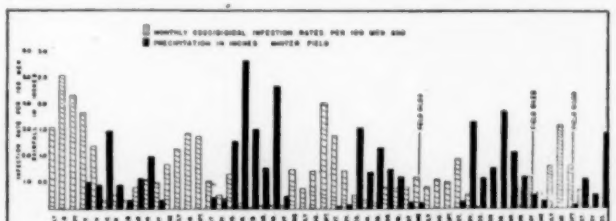

Fig. 4.—Monthly coccidioidal infection rate per 100 susceptible persons and precipitation in inches at Minter Field, 1941 to 1945.

in the multiplication of the fungus in nature, by whatever means this is accomplished. The immediate beneficial effect of rain in keeping the chlamydospores from blowing about in the air is obvious. Admittedly, the effect of heavy winter rainfall in providing abundant chlamydospores for inhalation in the succeeding summer is hypothetic.

3. (*a*) Ophüls, W., in discussion of papers by Cummins, Smith and Halliday and Pulford and Larson, J. A. M. A. **93:** 1055 (Oct. 5) 1929. Dickson, E. C., and Gifford, M. A.: Coccidioides Infection (Coccidioidomycosis): II. The Primary Type of Infection, Arch. Int. Med. **62:** 853-871 (Nov.) 1938. (*b*) Smith, C. E.: The Epidemiology of Acute Coccidioidomycosis with Erythema Nodosum ("San Joaquin" or "Valley Fever"), Am. J. Pub. Health **60:** 600-611 (June) 1940. (*c*) Davis, B. L.; Smith, R. T., and Smith, C. E.: An Epidemic of Coccidioidal Infection (Coccidioidomycosis), J. A. M. A. **118:** 1182-1186 (April 4) 1942. Goldstein, D. M., and Louie, S.: Primary Pulmonary Coccidioidomycosis: Report of an Epidemic of Seventy-Five Cases, War Med. **4:** 299-317 (Sept.) 1943. (*d*) Willett, F. M., and Weiss, A.: Coccidioidomycosis in Southern California: Report of a New Endemic Area with a Review of One Hundred Cases, Ann. Int. Med. **23:** 349-375 (Sept.) 1945.

4. Rixford, E.: Report of a Case Presented Before the San Francisco Medico-Chirurgical Society, March 5, 1894, Occidental M. Times **8:** 326 (May) 1894.

5. Emmons, C. W.: Isolation of Coccidioides from Soil and Rodents, Pub. Health Rep. **57:** 109-111 (Jan. 23) 1942.

6. (*a*) Giltner, L. T.: Occurrence of Coccidioidal Granuloma (Oidiomycosis) in Cattle, J. Agric. Research **14:** 533-541 (Sept. 16) 1918. (*b*) Beck, M. D.: Occurrence of Coccidioides Immitis in Lesions of Slaughtered Animals, Proc. Soc. Exper. Biol. & Med. **26:** 534-536 (March) 1929. (*c*) Beck, M. D.; Traum, J., and Harrington, E. S.: Coccidioidal Granuloma. Occurrence in Animals; Reference to Skin Tests, J. Am. Vet. M. A. **31:** 490-499 (April) 1931. Davis, C. L.; Stiles, G. W., and McGregor, A. W.: Coccidioidal Granuloma in Calves, ibid. **45:** 562-563 (April) 1938.

7. Farness, O. J.: Coccidioidal Infection in a Dog, J. Am. Vet. M. A. **97:** 263-264 (Sept.) 1940.

The pattern of maximal incidence in the first year of operation of the fields was seen at Lemoore. As table 2 indicates, the second year of operation at Lemoore provided an infection rate just one half that of the first season despite the fact that this was a heavy coccidioidal season, as indicated by an increase

TABLE 3.—*Monthly Incidence of Coccidioidomycosis in San Joaquin Valley Army Air Fields and Monthly Precipitation* in Inches, 1941 to 1945*

Date	Precipitation	Monthly Disease Rate per 1,000 Men, Minter	Monthly Infection Rate per 100 Susceptibles		
			Minter	Gardner	Lemoore
1941 July	0.00	0.10	3.17	1.08	....
August	Trace	0.41	5.12	1.89	....
September	0.00	0.55	4.47	2.39	....
October	0.53	0.45	3.75	4.00	....
November	0.49	0.17	2.47	3.44	....
December	1.54	0.00	0.38	2.22	....
1942 January	0.47	0.03	0.56	2.06	....
February	0.19	0.00	0.38	0.00	....
March	0.60	0.07	0.88	0.63	0.40
April	1.03	0.06	1.17	0.29	0.23
May	0.19	0.15	1.04	0.37	0.53
June	0.00	0.17	1.71	2.02	1.27
July	0.00	0.34	2.32	2.06	1.24
August	0.01	0.42	2.93	2.35	1.55
September	0.00	0.41	2.84	1.85	2.24
October	0.24	0.29	1.14	1.03	1.70
November	0.20	0.11	0.58	1.38	0.73
December	1.33	0.10	1.39	1.00	0.84
1943 January	2.87	0.02	0.22	0.87	1.12
February	1.55	0.04	0.07	0.30	0.58
March	0.80	0.00	0.13	0.15	0.00
April	2.39	0.00	0.19	0.00	0.08
May	0.25	0.00	0.18	0.37	0.41
June	0.00	0.23	1.52	0.12	0.16
July	Trace	0.35	0.81	0.57	0.47
August	0.00	0.43	1.45	3.09	0.39
September	0.00	0.87	4.10	1.86	0.00
October	0.05	0.81	2.85	3.04	0.75
November	0.09	0.42	1.49	1.46	1.04
December	1.58	0.28	0.53	0.02	1.17
1944 January	0.71	0.05	0.34	0.31	0.50
February	1.18	0.06	0.22	0.20	0.55
March	0.76	0.10	0.86	0.65	0.00
April	0.03	0.10	0.80	0.46	0.75
May	0.23	0.21	0.88	0.65	0.59
June	0.13	0.15	1.28	0.67	0.21
July	0.09	0.24	0.89	1.60	0.35
August	0.00	0.22	1.15	1.09	0.16
September	0.00	0.20	1.05	1.82	0.14
October	0.14	0.39	1.96	1.27	0.28
November	1.70	0.15	0.54	0.64	0.27
December	0.60	0.03	0.08	....	0.13
1945 January	0.82	0.00	0.00	....	0.00
February	1.01	0.00	0.00	....	0.24
March	1.15	0.00	0.00		
April	0.64	0.09	0.77		
May	0.26	0.22	1.29		
June	0.14	0.12	0.60		
July	0.00	0.29	1.62		
August	Trace	0.41	3.20		
September	0.07	0.25	1.65		
October	0.58	0.14	0.71		
November	0.28	0.18	0.79		
December	1.48	0.07	0.38		

* Precipitation data from U. S. Department of Commerce Weather Station, Kern County Air Port, Bakersfield, Calif.

over the previous year both at Minter and at Gardner. The improvements in local dust control more than offset more favorable conditions for Coccidioides.

After the relatively severe coccidioidal season of 1943-1944 at Minter and Gardner fields, concerted action was taken on other phases of dust control. The Board for the Investigation of Epidemic Diseases requested us to direct our attention to the problem. It was also receiving urgent study by the Air Surgeon's Office. At the fields the commandants, post surgeons, post engineers and Coccidioidomycosis Control Officers were working on the problem. With the encouragement and backing of Washington and the Ninth Service Command and Training Command, they took energetic steps.

It was recognized that in highly endemic areas coccidioidomycosis is bound to occur even if local dust control is reasonably effective. Dust blows in from areas surrounding an installation. Personnel do not stay on a post continuously. However, surfacing the roads, grassing the grounds and compelling personnel to use surfaced roads and walks rather than permitting them to wear away grassed areas and lawns greatly reduce the amount of local dust. The Pacific Division of Ninth Service Command U. S. A. Engineers prepared an excellent treatise on agronomy in passive protection from dust.

Two additional steps were taken. More swimming pools were constructed so that, as much as was possible, aquatics were substituted for other forms of exercise. Indeed, the principal areas left without turf were fields used for calisthenics, baseball, volley ball and other forms of physical training. Some of these areas had an asphalt (blacktop) surface, but asphalt is not only expensive but also hard on feet during the extremely hot weather. The use of crushed rock and gravel was out of the question because of injuries which would ensue. These activities could not be abandoned completely, while control of dust in those areas seemed especially important since with exercise there is deeper breathing and an increase in the amount of air actually inspired. Therefore, an attempt was made to control the dust by the use of oil. Crude oil forms a crust which breaks up in lumps. Moreover, unless it is highly refined oil stains skin and clothing and is apt to be irritating. However, a number of highly refined oils are available. Such oil penetrates the upper inch of soil, impregnating the particles of dirt. Then even if the treated soil breaks up into dust and is scuffed, the oiled particles fall back to the ground instead of being blown about in clouds.

Accordingly, in May 1944, both Gardner and Minter fields embarked on the use of oil for athletic areas. Gardner's first attempt in early May was unsuccessful. Initially it was thought the failure was due to a preliminary disking. While it is true that the more heavily the soil is packed the better, the major fault proved to be in the character of the soil. Gardner Field was built on the fine silt of an old lake bottom. Even with a second, heavier application in June, the oil crust broke through and unoiled dust was exposed.

The soil at Minter Field, heavier and with more clay, proved more suitable. Preliminary tests were run on volley ball courts to estimate oil dosage. It was observed that 1 quart of oil per square yard was optimal. The oil was applied in late May and early June. While the dust control was only moderately effective at Gardner Field for a few weeks after each oil application, at Minter Field it seemed reasonably satisfactory until October. Fortunately, as it was wearing off, late October rains terminated the coccidioidal season.

The effect of the oiling is seen in table 3 and figures 3 and 4. It is to be recalled that oil was applied to Gardner Field in early May and again in late June 1944, while athletic areas at Minter were oiled in late May and early June 1944. Also, by October the effect

of oiling had largely worn off at Minter. The low incidence at Minter may be partially attributed to the preceding dry winter; however, not only was the Minter rate the lowest in its experience but also, for the first time, the June through November rate was below that of Gardner. During that six month period the infection rate at Minter was 6.87 per 100 susceptible persons, while that at Gardner was 7.69. Although this difference is not spectacular, in 1943 the same six months provided a 12.22 infection rate at Minter compared with that of 10.14 at Gardner. In 1942 the rate was 11.52 at Minter and 10.68 at Gardner. During the five months July through November 1941, it was 18.98 at Minter and 13.40 at Gardner. During 1942 and again in 1943 the Minter rate exceeded the Gardner rate in four of those six months; in 1944 the Gardner rate exceeded Minter in four of the six months. Minter was below the Gardner rate only this one season when oiling succeeded at Minter and failed at Gardner.

Another item of evidence was available. In the six months of summer and autumn of 1943, the Minter Field medical detachment enlisted personnel suffered 15 coccidioidal infections. The number of susceptible persons was an even 100, so the infection rate was 15 per 100 men. Athletic fields were behind the station hospital, with the barracks of the enlisted men directly at the edge of the athletic areas. In the same period of 1944 only 2 infections were acquired. Forty-two of those persons originally negative at the beginning of the six months were still present at the retest. The infection rate calculates to 5 per 100 men. Admittedly, the numbers are small, but the trend coincides with the rest of the evidence.

The closing of Gardner Field eliminated subsequent comparison. However, the 1945 experience at Minter provided additional evidence. After a record-breaking initial three months without any infections, cases appeared in April and by mid-May were increasing rapidly. The post engineer acceded to the pressure and began the application of oil on May 20. He had been reluctant because he feared late rains and knew that rains would render the oil less permanent. His fears were justified, for only a week after the oil was applied it began to rain and rained a total of 0.33 inch. The combination of oil and rain did drop the coccidioidomycosis, but because the rain had interfered with the durability of the oiling, by August the areas were extremely dusty. August provided a rate nearly twice that of any month in 1944 and exceeded only once since 1941. Oil was reapplied the first week in September with immediate cessation of coccidioidomycosis.

The most dramatic tribute to the efficacy of the Minter dust control was a comparison with members of two camps of agricultural workers in the same region. Only clinically diagnosed, hospitalized cases could be compared, but with the availability of diagnostic facilities at Minter Field it is conservative to consider that the clinical diagnoses were made with as great care and our Army personnel were hospitalized in no greater proportion than were the agricultural workers. Within a two month and ten day period extending from June into August, 22 Minter Field personnel were hospitalized for coccidioidomycosis compared with 150 agricultural workers. The field strength at Minter was approximately 3,400, while there were only 1,500 agricultural workers.

Working with different data, Major Howard B. Sprague has assembled decidedly convincing evidence of the beneficial effect of dust control on coccidioidal incidence.[8] One of his most telling items was a comparison of the incidence of coccidioidomycosis at Davis-Monthan Field and at Marana Army Air Base. Both fields are located near Tucson, Ariz., and have comparable soil and climate. Until 1944 the incidence of coccidioidomycosis was similar. In that year dust continued unabated at Marana and coccidioidomycosis soared in the summer and autumn. However, strict dust control was inaugurated at Davis-Monthan early in 1944. These measures were successful and were followed by almost complete elimination of hospital cases of coccidioidomycosis during the summer and autumn.

COMMENT

The seasonal infection rate of coccidioidomycosis again evinces that dust is the mechanism by which the fungus is transported. Even where the coccidioidal infection rate is 5 to 10 per cent per year, it is easy to understand why most of the long-time inhabitants have been infected. It is doubtful if a community in such an area could profitably essay complete dust control in order to prevent coccidioidomycosis among its citizens. However, lawns, parks, paved roads and dust-free playgrounds are pleasant, especially in the hot regions where Coccidioides flourishes. Certainly, sanatoriums located in coccidioidal endemic areas to take advantage of the warm dry climate should have the benefit of dust control measures.

In the special conditions which prevail in army camps in coccidioidal areas, where large numbers of susceptible persons are being introduced and those infected are departing as fast as they are becoming immune, local dust control seems warranted. Whenever feasible, grassing should be used. The surfacing of roads and, to a limited degree, that of athletic areas is important. However, many athletic areas cannot be surfaced because of heat on the feet and the danger of injuries after falls. If turf cannot be maintained on the areas, the application of a highly refined oil may be tried. However, one should first examine the character of the soil. If the soil is a fine loose silt like that of Gardner Field, success is unlikely. If it is a heavy adobe type, the outlook is favorable. In any event, one should run preliminary tests to prove effectiveness, to decide on the product to be used and to fix the quantity to be applied. In addition, every effort should be made to develop an aquatic physical training program during the suitable hot months, which will correspond with the season of high coccidioidal exposure.

SUMMARY

The monthly and yearly rates of coccidioidal infection were calculated in susceptible (coccidioidin negative) personnel of four San Joaquin Valley army air fields. The results emphasized the geographic distribution of the endemic area and the importance of dust in infecting man with Coccidioides immitis. At the most northerly station the annual infection rate was only 0.5 per 100 susceptible persons compared with 20 to 25 at the two southerly fields when dust was uncontrolled. Maximal incidence occurred in the arid dusty summer and

8. Sprague, H. B.: Summary of the Relation Between Occurrence of Dust and Incidence of Coccidioidomycosis (Valley Fever) at Army Air Fields in California and Arizona, Memorandum to Army Air Force Headquarters, Oct. 1, 1945.

autumn, a single month providing 5 per cent of the infections. Grassing, paving roads and runways and ultimately the use of highly refined oil on athletic areas were important dust control measures. This control reduced infection rates from one half to two thirds.

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ABSTRACT OF DISCUSSION

DR. RUSSELL V. LEE, San Francisco: Dr. Smith and his associates know more about coccidioidomycosis than any one else, and this work with the Army Air Forces and Ground Forces was a most remarkable piece of combined epidemiology and curative medicine. They surveyed every man in that important military area, important because most of the training fields for the Army Air Forces were located within the area where coccidioidomycosis is prevalent. Dr. Smith was of great help in outlining the problems which might be encountered, and one type threatened to be a considerable menace. It was shown in the paper that dust control could remarkably reduce the incidence of the disease in an area where, left alone, in a year or two the incidence of infection would increase remarkably, and after a number of years' residence in the area we were practically 100 per cent uninfected with coccidioidomycosis. While the mortality was very low, it was the principal cause of hospitalization in many of the Air Force hospitals in that southwest area, so that anything that can be done to reduce it under such circumstances should be done. The incidence under military conditions, particularly under air conditions, was very high. The airplane propeller picks up a lot of dust; soldiers around camps and marching in physical training kick up a lot of dust, and they have become infected at a terrific rate. There was a hospital at San Benito where about one fourth of the men of one detachment were hospitalized and thus saved from going back to this exceedingly dusty region right in the middle of the season of highest incidence. This has lessons for civilian application. This whole desert area has been outlined now largely by the work of Dr. Smith. He can draw a very accurate line around the endemic area of coccidioidomycosis. It is a much larger area than was ever dreamed of before, and when certain types of activities are going to be carried out in that area certain precautions will have to be adopted to protect against coccidioidomycosis. For instance, we had Negro troops in that area, and the Negro is many times more susceptible to coccidioidomycosis than the white man. Negroes should be kept out of that area and the dusty occupations there. It is definitely a hazard for them, judging by the army experience there. In due time there is going to come from Dr. Smith's work the most comprehensive, complete definition of the clinical features as well as the epidemiologic features of coccidioidomycosis. The knowledge of this disease is exactly 50 years old, but in the last five years the whole thing has crystallized. Papers and monographs undoubtedly will appear shortly as a result of this army experience, and this disease is going to be defined with a precision with which it has never been defined before.

Postwar Malaria.—In continental United States civilian malaria in the aggregate is at an all time low; there has been little perceptible change in the past five years. Available data show a marked decrease in malaria rates among continental military personnel since 1941, but in these figures is reflected the extensive control programs in military areas. The cyclic upswing predicted for the early forties by some malariologists has not occurred. In the past two decades reported malaria mortality and morbidity have dropped 85 per cent and 70 per cent respectively.—Hollis, Mark D.: Postwar Malaria Control in Continental United States, *J. Nat. Malaria Soc.*, June 1946.

RADIOACTIVE IODINE THERAPY

Effect on Functioning Metastases of Adenocarcinoma of the Thyroid

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Therapy of neoplastic disease usually consists of two phases: first, the treatment of the primary focus and, second, that of metastases. Specifically, in adenocarcinoma of the thyroid, the primary site together with its immediate extensions is conventionally treated by surgery, radiation or both. Distant metastases, if treated, are usually subjected to palliative external irradiation. This paper is a report of successful therapy of a case of metastatic adenocarcinoma of the thyroid treated by the principle of specific internal irradiation with radioactive iodine.

The earliest study of the uptake of radioactive iodine in 2 cases of carcinoma was reported by Hamilton and his associates [1] in 1940. In 1942 he described 2 more cases [2] in which tracer doses of radioactive iodine had been given to the patients prior to the removal of carcinomatous thyroids. Radioautographs of the excised glands showed no significant deposition of the radioactive iodine in malignant areas in any of these cases.

In April 1942, Keston, Ball, Frantz and Palmer [3] reported the first positive evidence of pickup of the radioactive iodine by a metastasis from a carcinoma of the thyroid. In a patient with multiple lesions, Geiger counter measurements showed appreciable uptake of radioactive iodine in only one of the metastases. Subsequently, from the autopsy, these authors [4] reported that "the bulk of the metastatic tissue was undifferentiated. The metastasis which showed consistent uptake of iodine was the only one which grossly resembled thyroid tissue and which, microscopically, showed chiefly well differentiated tumor."

Leiter, Seidlin, Marinelli and Baumann [5] in a report of 2 cases (1 of which is the subject of the present paper) of hyperthyroidism due to adenocarcinoma of the thyroid and to functioning metastases showed that the effect of thiouracil on the basal metabolic rate, plasma cholesterol, blood iodine and excretion of radioactive iodine in these patients was in every respect

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A preliminary report of this work was presented at the Clinical Research Meeting of the New York Academy of Medicine on May 16, 1945.

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The cooperation of the staffs of the Massachusetts Institute of Technology and Washington University cyclotrons and of Dr. R. D. Evans made this work possible.

Dr. Louis Leiter, Chief of the Medical Division of Montefiore Hospital, gave valuable assistance throughout this work, as did Dr. David Marine and Dr. S. H. Rosen in the field of thyroid pathology and Dr. E. J. Baumann in iodine chemistry. Dr. Solomon Fineman reviewed the roentgenograms. Valuable technical assistance was rendered by Elizabeth F. Focht, Ruth Hill, George Ross, Louella Tulip and Dr. A. A. Yalow.

1. Hamilton, J. G.; Soley, M. H., and Eichorn, K. B.: Deposition of Radioactive Iodine in Human Thyroid Tissue, Univ. California Publ., Pharmacol. **1**: 339-368, 1940.

2. Hamilton, J. G.: The Use of Radioactive Tracers in Biology and Medicine, Radiology **39**: 541-572 (Nov.) 1942.

3. Keston, A. S.; Ball, R. P.; Frantz, V. K., and Palmer, W. W.: Storage of Radioactive Iodine in a Metastasis from Thyroid Carcinoma, Science **95**: 362-363 (April 3) 1942.

4. Frantz, V. K.; Ball, R. P.; Keston, A. S., and Palmer, W. W.: Thyroid Carcinoma with Metastases: Studied with Radioactive Iodine, Ann. Surg. **119**: 668-669 (May) 1944.

5. Leiter, L.; Seidlin, S. M.; Marinelli, L. D., and Baumann, E. J.: Adenocarcinoma of the Thyroid with Hyperthyroidism and Functional Metastases: I. Studies with Thiouracil and Radio-Iodine, J. Clin. Endocrinol. **6**: 247-261 (March) 1946.

similar to the response already described [6] in the literature on ordinary thyrotoxicosis or hyperthyroidism. This indicates that thiouracil suppresses hormone production by functioning metastases from adenocarcinoma of the thyroid as readily as it inhibits this process in the hyperplastic thyroid of ordinary hyperthyroidism.

Since physiologically the thyroid cell, normal or malignant, cannot distinguish between inert and radioactive iodine, we are utilizing the normal affinity of this cell for iodine as a method of "selective irradiation" of a type of carcinoma of the thyroid. We now report the results of three years' study of the therapeutic effect of radioactive iodine in 1 case of metastatic carcinoma of the thyroid, in which all demonstrable metastases were shown to pick up radioactive iodine.

Radioactive iodine, as used in this and similar studies, consists of a mixture, in varying proportions, of two isotopes, I^{130}, half life 12.6 hours, and I^{131}, half life 8.0 days, prepared in a cyclotron by the bombardment of tellurium with deuterons. These two isotopes are chemically identical with stable iodine and cannot be separated by ordinary chemical or physiologic methods and processes. Both I^{130} and I^{131} emit beta rays (high speed electrons) which cause intense ionization within a few millimeters of tissue, as well as gamma rays which cause a negligible amount of ionization within the body and are sufficiently penetrating to be detected readily by an external Geiger counter.

REPORT OF CASE

Observations Prior to Radioactive Iodine Therapy.—Thyroidectomy: B. B., a man aged 51, had in 1923, at the age of 30, undergone a thyroidectomy because of substernal goiter and pressure symptoms on the trachea. He had no thyrotoxicosis. The histologic diagnosis was "malignant adenoma."

Pathologic Report: The pathologic report gave a gross description of three pieces of tissue received. The first one measured 5 by 5 by 3 cm. It was firm in consistency, and the cut section showed a fairly dense central core of connective tissue. No cystic or hemorrhagic areas were observed. The outer portion of the section disclosed a brownish yellow semipurulent material. The remaining two pieces of tissue were relatively the same in general structure but averaged about 2.5 cm. in thickness.

On microscopic examination, sections of the goiter showed no normal structures. Sections of tissue revealed definite fibrous change and there was an abundant pinkish hyaline-like stroma manifesting cell formation. There was a definite, highly atypical epithelial overgrowth which showed abundant growth and a tendency toward cord formation. In these areas no acini resembling the normal were seen. The nuclei of the cells took a rich blue stain. The growth showed no definite capsule surrounding it. Areas showing cartilage formation were present. No hemorrhage or infection was observed.

Recurrence and Laminectomy: Postoperatively there were no symptoms of hypothyroidism. The patient was in apparent good health for fifteen years. Then there developed palpitation, nervousness, loss of weight and signs typical of hyperthyroidism. In addition, severe pains developed in the lower back and radiated down the legs. On examination at another hospital in October 1939, a small pulsating tumor was found in the midline of the back at the level of the twelfth thoracic vertebra. Visualization by injection of diodrast showed the tumor to be extradural and extraosseous. Roentgenograms of the skeleton revealed no osseous lesions. The basal metabolic rate was + 40 per cent. A laminectomy was performed in November 1939. The tumor proved to be a metastatic carcinoma of the thyroid (fig. 1).

The histologic report revealed that the slide [7] showed several large ragged fragments of tissue, one of which contained spicules of bone and consisted of irregular cellular areas formed by broad hyalinized stroma bands. The general pattern was the same in all portions and consisted of irregular, often elongated, closely packed follicles with infoldings of the lining epithelium which varied from cuboidal to low columnar. There was no well formed stroma. Traces of granular colloid-like material were present in some follicles. In some areas the follicles appeared to have atrophied leaving the hyalinized-like bands previously mentioned. There were large areas of necrosis and some foci of hemorrhage. No mitosis was seen.

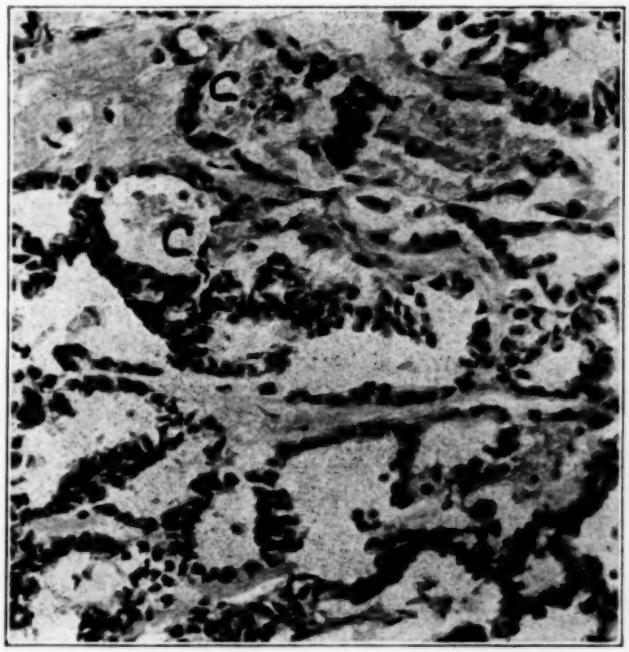

Fig. 1.—Photomicrograph of metastatic tumor in the twelfth thoracic vertebra magnified 400 times. Note follicular architecture and traces of granular colloid-like material (*c*) in some follicles.

The nuclei were fairly regular, dark and vesicular. The diagnosis was metastatic adenocarcinoma of the thyroid.[8]

Treatment and Course: A thyroid crisis developed postoperatively. A few weeks later an exploratory operation was performed in the region of the thyroid and no thyroid tissue, normal or malignant, was found. Because of continuing pain, physiotherapy was given to the patient. In the next two years the symptoms and signs of hyperthyroidism increased. In December 1941 the basal metabolic rate was + 45 per cent. In addition, roentgen ray films of the lungs revealed "numerous circular deposits in the lower lobe on the left side and in the cardiohepatic angle on the right side, strongly suspicious of metastatic lesions." There was also radiographic evidence of destruction of the right upper femur (1.0 by 2.0 cm.) and the second rib on the left side. A gastrointestinal roentgenologic series was negative. A film of the pelvis taken at this time was reported negative for metastases, but our subsequent review (1946) of the plate revealed a small area (0.6 by 1.8 cm.) of early destructive changes in the inner border of the left ileum, above the acetabulum, just below the incisura ischiadica major. From December 1941 to February 1942 high voltage

6. Mackenzie, C. G., and Mackenzie, J. B.: Effect of Sulfonamides and Thioureas on the Thyroid Gland and Basal Metabolism, Endocrinology **32**: 185-209 (Feb.) 1943. Astwood, E. B.: The Chemical Nature of Compounds Which Inhibit the Function of the Thyroid Gland, J. Pharmacol. & Exper. Therap. **78**: 79-89 (May) 1943. Williams, R. H., and Bissell, G. W.: Thiouracil in the Treatment of Thyrotoxicosis, New England J. Med. **229**: 97-108 (July 15) 1943. Williams, R. H., and Clute, H. M.: Thiouracil in the Treatment of Thyrotoxicosis, ibid. **230**: 657-667 (June 1) 1944. Rawson, R. W.; Evans, R. D.; Means, J. H.; Peacock, W. C.; Lerman, J., and Cortell, R. R.: The Effect of Thiouracil on the Thyroid Glands of Patients with Graves' Disease, J. Clin. Endocrinol. **4**: 1-11 (Jan.) 1944. Franklin, A. L.; Chaikoff, I. L., and Lerner, S. R.: The Influence of Goitrogenic Substances on the Conversion in Vitro of Inorganic Iodine to Thyroxine and Diiodotyrosine by Thyroid Tissue with Radioactive Iodine as Indicator, J. Biol. Chem. **153**: 151-162 (April) 1944. Rawson, R. W.; Tannheimer, J. F., and Peacock, W. C.: The Uptake of Radioactive Iodine by the Thyroids of Rats Made Goitrous by Potassium Thiocyanate and by Thiouracil, Endocrinology **34**: 245-253 (April) 1944.

7. Courtesy of Dr. H. L. Jaffe, Hospital for Joint Diseases.
8. The slide was reviewed by Dr. David Marine.

roentgen therapy was administered[9] as follows: dorsolumbar spine, 4,060 r; right upper femur, 3,180 r delivered through three fields. This course of therapy did not produce any symptomatic improvement.

Radioactive Iodine Therapy.—Observations at Hospitalization: On admission to Montefiore Hospital on April 20, 1942, the patient still had symptoms of pain in the lower part of the spine, in addition to the previously mentioned symptoms of hyperthyroidism.

The physical examination showed a rather small, emaciated, poorly developed man, aged 48, weight 38 Kg. and height 146 cm.; he was hyperkinetic, his blood pressure was 128 mm. of mercury systolic and 50 diastolic; his pulse rate was 100 to 110. There were no eye signs. There was a thyroidectomy scar in the neck, and no thyroid tissue was palpable. The heart was normal except for tachycardia. The lungs were clear. There was a laminectomy scar and tenderness over the dorsolumbar spine. The eye grounds were normal. The skin was warm, and there was a coarse tremor of the hands. The basal metabolic rate on May 7, 1942 was + 36 per cent. The plasma cholesterol about this time was 114 mg. per hundred cubic centimeters and the blood iodine[10] soon thereafter was 11.9 micrograms per hundred cubic centimeters.

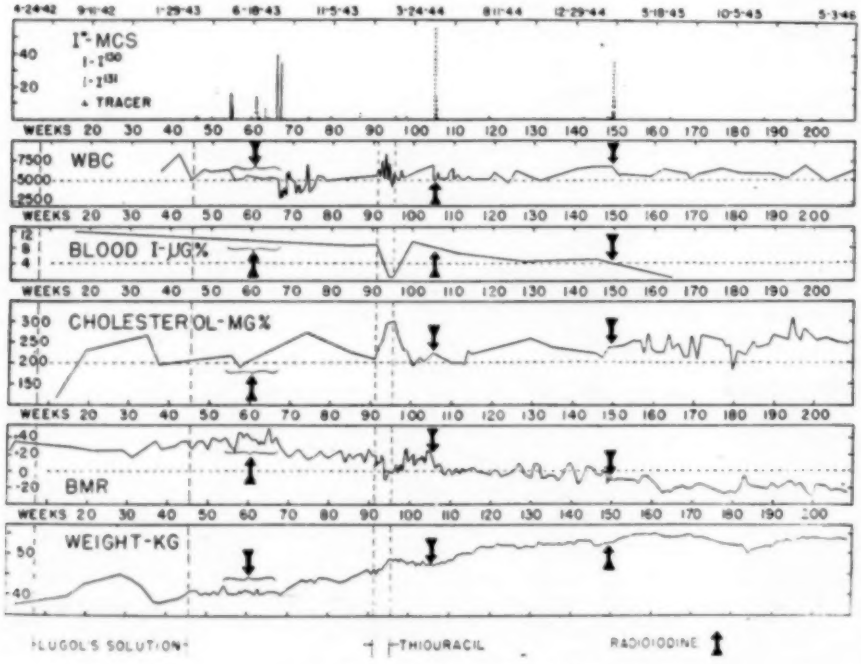

Fig. 2.—Response of clinical criteria to the administration of I *.

Other laboratory examinations revealed nothing of special significance. The blood chemistry tests showed calcium, 10.3 mg., and phosphorus, 3.9 mg. per hundred cubic centimeters; phosphatase (alkaline) 12.2 Bodansky units; total serum protein, 6.7 Gm.; serum albumin, 3.2 Gm.; serum globulin, 3.5 Gm., and uric acid, 3.9 mg. per hundred cubic centimeters. The Wassermann and Kahn tests were negative; the blood count was within normal limits. Urinalysis was negative. The Ewald test showed free hydrochloric acid, none; combined acid 20 per cent.

A roentgenologic examination of the chest on April 25, 1942 revealed several rounded shadows suggestive of metastases in the lower lobe of the left lung; an extensive destructive lesion (5 cm. long) which involved the lateral and posterior aspect of the second rib on the left side; a circumscribed shadow (3.2 by 1.1 cm.) in the left infraclavicular region, which seemingly arose from the involved rib and represented a soft tissue mass. A picture of the dorsolumbar spine on Nov. 10, 1942 disclosed evidence of laminectomy; the spinous processes of the eleventh and twelfth thoracic vertebrae and the first lumbar vertebra were missing, and osteoporosis involved all the vertebrae. The pelvis on April 25, 1942 showed a small area of bone absorption (0.6 by 2.3 cm.) along the medial aspect of the left ileum above the acetabulum. The femurs on Oct. 29, 1942 presented a small area (larger than in films of December 1941) of bone absorption in the cortex of the right femur just below the lesser trochanter.

In view of the evident hyperthyroidism, iodine as Lugol's solution was administered every day in doses varying from 1 to 6 cc., from June 13, 1942 to March 8, 1943.[5]

As shown in figure 2, a mild remission in the hyperthyroidism occurred in response to the iodine therapy. By January 1943, iodine given as Lugol's solution in doses of 3 to 4 cc. a day lost its effectiveness even in regard to the hyperthyroidism itself, and its continued administration produced little further improvement.

The lesions of the bone continued to grow, and pain persisted. Another course of roentgen therapy was instituted as follows: right upper femur 3,260 r through two fields, and left pelvis 1,985 r through two fields. There was no relief of pain.

Administration of Radioactive Iodine: In March 1943 a tracer dose of radioactive iodine was given orally in the form of sodium iodide in water. This method of administration has been used for all doses. Geiger counter measurements revealed iodine retention by all the known lesions plus two previously unsuspected ones (fig. 3); one in the skull and one, not evident in the roentgenograms, located in the region of the ischium. During the taking of Geiger counter measurements, the patient asked that the counter be placed on the right parietal part of his head, for, he stated, there is a pain there which "is not a headache." Surprisingly, the counter registered the uptake of radioactive iodine. A subsequent roentgenogram (May 18, 1943) of the skull was reported as disclosing a fairly sharply circumscribed area of bone rarefaction (3.7 by 3.5 cm.) in the right posterior parietal region. At this time an exhaustive study of radioactive iodine uptake in the neck was made, and no evidence of residual functioning thyroid tissue could be established (see later comment). Due to technical difficulties, no attempt was made to study the radioactive iodine content of the lung metastases reported by the roentgen ray diagnostic department.

Measurements on urine after several tracer doses revealed that the patient excreted a relatively small amount (30 per cent to 40 per cent) of the tracer dose over a seventy-two to ninety-six hour period. The first course of radioactive iodine therapy, a total of 102 millicuries of the 12.6 hour isotope (I^{130}) and 20.5 millicures of the 8 day isotope (I^{131}), was administered between May and August, 1943 (see the accompanying table). The estimated radiation dose[11] to the tumors was 10,600 equivalent r,[12] whereas that for the blood was 70 equivalent r.

Since this course was administered in fractions of varying potency, it was possible to determine the effect of the different radiation doses on the leukocyte count. The I^{131} had no

9. Radiation dosages in this paper refer to tumor doses exclusively. Tumor depths were estimated from roentgenograms. Data used here were obtained from Rosh, R., and Raider, L.: Radiation Therapy of Carcinoma of the Thyroid, Radiology **44**: 556-564 (June) 1945 and a personal communication from Dr. Rosh.

10. Baumann, E. J., and Metzger, N.: On the Amount of Iodine in the Blood, J. Biol. Chem. **121**: 231-234 (Oct.) 1937.

11. This dose and the following therapeutic doses are calculated on the basis of an effective tumor volume of 312 cc. (vide infra) and on the basis of I * (I * refers to radioactive iodine without specifying the isotope) retained; that is, that administered minus that excreted in the urine. The possible change in effective tumor volume with time has been neglected. It would have been preferable, and is planned in the future to estimate tumor dose by actual measurements in vivo.

12. Equivalent roentgens as used herein are defined and discussed in Marinelli, L. D.: Dosage Determinations with Radioactive Isotopes, Am. J. Roentgenol. **47**: 210-216 (Feb.) 1942.

significant effect while the I^{130} had a considerable, though temporary, depressing influence (fig. 2). The expanded curve, figure 4, shows that after one dose of 40 millicuries of I^{130} the white blood cell count dropped from 5,150 to 2,900 in one week. The blood count returned to normal in ten days even though another dose of 35 millicuries of I^{130} was given while the count was low.

The resulting improvement in the patient's clinical picture was definite in the course of the next few months. By November 1943 the pains diminished, the basal metabolic rate dropped from an average level of above + 35 per cent to about + 20 per cent, the patient gained about 7 Kg. in weight and roentgenologically there was no demonstrable growth of the metastases.

Biopsy: On Nov. 6, 1943, a dissection biopsy of the metastasis in the second rib on the left side was performed by Dr. A. H. Aufses. In order to obtain a radioautograph of this lesion and to ascertain the radioactive iodine concentration in the tumor tissue, a large tracer dose of I^{131} (5 millicuries) was administered eight days before the operation. To remove the tumor on the second rib on the left side it was necessary to perform a scapula-mobilizing incision, with

From these figures and from the total urinary excretion up to the time of the biopsy it is possible to calculate the apparent tumor weight in the patient, assuming that the iodine concentration is uniform throughout the metastases and that no appreciable radioactive iodine is present in nontumorous tissues. This value is 312 Gm. It is interesting to note at this point that an independent calculation of the tumor volume based on the contour of the metastases in the roentgen ray films agrees with the above value.

A comparison of the biopsy tissue (figs. 5 and 9) with a section of the tissue removed on laminectomy in October 1939 (fig. 1) revealed close similarity.

Pathologic Report: The pathologic report was as follows: On macroscopic examination the fresh specimen was an oval mass measuring 7.5 by 4.3 by 2.5 cm. and weighing 41.9 Gm. It was enclosed in a grayish white capsule about 0.5 cm. thick on the surface of which there were, in places, some fibrofatty tissue and muscle. Attached to the capsule on one surface there was a piece of rib measuring 3.5 cm. in length to which was attached some fragments of muscle and fascia. The mass was moderately soft, rather rubbery in consistency. On section, the tissue presented a mottled appearance, predominantly pale brownish with small and larger irregular dark red areas of congestion and hemorrhage, small translucent gray and yellowish foci and a few small, opaque, yellowish areas, probably of necrosis. Some thin grayish white strands of fibrous tissue could be seen running through the mass. The portion of rib attached to the mass was invaded on its adherent surface by tumor similar to and continuous with that of the mass, and fine bony spicules could be palpated in the latter for a distance of 1 cm. or more from the rib.

Microscopic examination revealed that the specimen consisted of sections of the tumor fixed in solution of formaldehyde and in Orth's solution and of decalcified portions of the tumor which included invaded rib. The tumor was surrounded by a thick capsule of dense fibrous tissue covered by fibrofatty tissue containing striated muscle fibers as well as some nerves and thickened arteries. The muscle fibers showed considerable atrophy and degeneration. Occasional focal infiltrations of small round cells were seen. The rather extensive hemorrhage in the capsule and surrounding tissue was probably largely traumatic. There was slight invasion of the capsule by tumor in a few places. In all sections the central two thirds or more of the tumor showed

Complete Tabulation of I Administered*

Date	Week	Iodine: Carrier (Mg.)	Iodine: Radioactive (Mc.)	Isotope	Excretion, per Cent per 24 Hours: 1	2	3	4	Remarks
3/11/43	45	0.15	Tr.‡	....	60.0	7.5	1.8	0.5	Iodine as lugol's solution 6/13/42 to 3/8/43
4/ 6/43	49	?	Tr.	....	25.0	15.0	...	...	
5/11/43	54	<0.5	17	I^{130}	11.7	...	...	...	
5/12/43	54	?	7.6	I^{130}	....	...	...	...	
6/15/43	59	0.3	2	I^{130}	14.1	3.0	...	...	
6/23/43	60	Neg.	13.5	I^{131}	26.8	2.6	...	...	
6/28/43	61	?	Tr.	....	....	...	...	...	
7/ 9/43	63	?	7.0	I^{131}	19.5	3.3	2.7	2.5	
7/15/43	63	?	Tr.	....	....	...	...	...	
7/29/43	65	<0.5	40.0 †	I^{130}	20.3	4.1	3.4	3.1	3 day stool, 2.3 per cent
8/ 5/43	66	<0.5	35.0 †	I^{130}	39.3	5.3	4.1	3.7	
9/22/43	73	Tr.	Tr.	....	15.1	1.6	2.3	2.8	
10/30/43	79	Tr.	2.0	I^{131}	27.4	4.4	2.9	2.8	
12/19/43	86	0.3	5.0	I^{131}	33.6	8.6	1.2	2.1	Pre-biopsy
2/21/44	95	0.03	Tr.	....	79.2	3.7	1.7	1.4	Thiouracil 1/23/44 to 2/21/44
3/10/44	98	0.1	Tr.	....	32.0	2.6	2.2	1.8	
4/28/44	105	2.5	55.4 † / 3.2 †	I^{131} / I^{130}	45.9	...	...	...	Blood curve taken
4/29/44	105	?	13.8	I^{131}	....	...	...	...	Refeeding
4/30/44	105	?	6.3	I^{131}	....	...	...	...	Refeeding
8/ 2/44	118	0.25	Tr.	....	26.0	2.8	1.3	1.0	
1/13/45	142	<0.2	Tr.	....	45.4	3.5	1.4	1.9	
2/23/45	148	<0.5	Tr.	....	?	?	?	?	Thyrotropic hormone 2/8/45 to 2/25/45
3/ 2/45	149	0.01	Tr.	....	34.1	...	...	...	
3/ 3/45	149	1.0	41.6 † / 6.0 †	I^{131} / I^{130}	54.3	7.7	1.6	...	Blood curve taken
3/ 6/45	149	?	13.4	I^{131}	....	...	...	...	Refeeding
6/11/45	163	0.3	Tr.	....	59.0	8.2	1.9	1.7	
11/24/45	187	<0.002	Tr.	....	59.8	10.6	0.9	...	
1/21/46	195	<0.04	Tr.	....	54.9	8.1	1.3	1.2	
2/ 6/46	201	14.0	Tr.	....	74.7	12.4	1.9	0.4	Large amount of carrier iodine

* I* refers to radioactive iodine without specifying the isotope.[11]
‡ Tr. indicates a tracer dose.
† Measurements of initial activity in millicuries carefully carried out.

incision through the muscles of the posterior chest wall. The postoperative course was uneventful, and the patient made an excellent recovery.

Several radioautographs of the biopsy specimen were obtained by following in general the technic already described by Hamilton.[2] Figure 6 shows a representative radioautograph and figure 7 is the eosin and hematoxylin stained section from which it was made. A superimposition[13] of these two photographs is shown in figure 8. A detailed comparison between radioautograph and photomicrograph shows specific localization of the radioactive iodine within the regions of viable thyroid tumor cells.

The total iodine content per gram of dry tissue of the biopsy specimen was 0.192 mg. with a thyroxin fraction of 17.4 per cent. The radioactive iodine content of the tumor tissue at the time of the biopsy was determined on four separate fresh specimens, weighing 0.28, 0.17, 1.49 and 2.05 Gm., respectively. The results were 0.18, 0.16, 0.19 and 0.20 per cent of the administered dose per gram of wet tissue.[14]

13. This composite photograph was made by John M. Walke of the Physics Department of Memorial Hospital.
14. Dr. Albert Keston made an independent determination on two of the specimens.

extensive necrosis, hemorrhage and edema. This portion of the tumor consisted largely of fibrinous material which in areas was loose and fibrillar and in other places, dense and hyaline-like. Mixed with this in varying amounts were edema fluid, red blood corpuscles and in a few foci, necrotic and disintegrating polymorphonuclear leukocytes. Small and larger foci of viable tumor, frequently compressed, distorted and

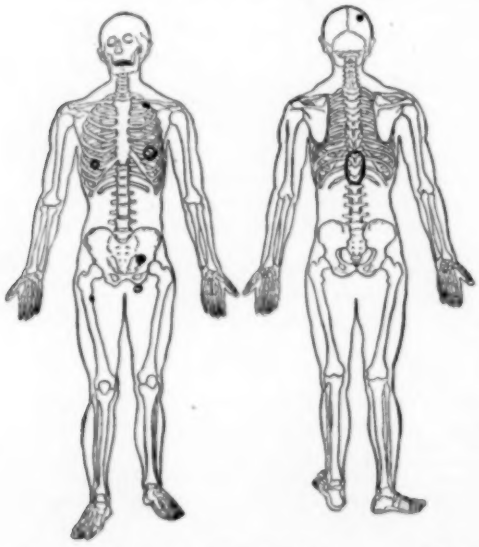

Fig. 3.—Location of metastases; solid black areas indicate osseous lesions, open circles indicate extraosseous lesions.

degenerating, were also seen in this central area. In places bands of edematous and hyaline-like stroma covered by flattened cells separated islands of fibrinous material, and in other places spindle cells growing in this material suggested organization. The peripheral, viable portion of the tumor disclosed little variation in architecture. It consisted of well differentiated follicles which disclosed considerable variation in size and shape but were predominantly small. The larger ones frequently showed infoldings and occasionally buds of new follicles in the walls. Some were widely dilated and others, compressed and slitlike. The follicles were lined for the most part by fairly uniform large cuboidal cells and in many instances by columnar cells. These cells had abundant acidophilic cytoplasm and fairly large, round, usually central but frequently basal, vesicular and hyperchromatic nuclei with

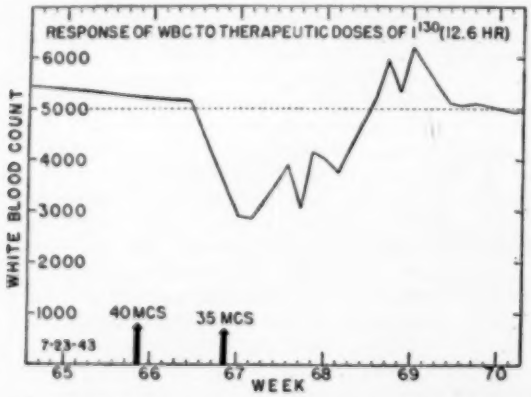

Fig. 4.—Effect of large amounts of I^{130} on the white blood cell count.

fairly large nucleoli. No mitotic figures were seen. The nuclei on the whole were uniform, but an occasional large hyperchromatic nucleus was seen as well as occasional small pyknotic ones. In large areas the abundant cytoplasm was deeply acidophilic, and the cells resembled the so-called Hürthle cell. In some areas distended follicles were lined by low cuboidal or flattened epithelium. Although most of the follicles were empty or contained some red blood corpuscles and fibrin-like material, a considerable number contained a homogeneous colloid-like material which took a pale pink stain. In some areas the follicles were closely packed and separated only by narrow strands of connective tissue which contained many thin-walled sinusoid-like vascular channels, frequently engorged. In other areas the connective tissue septums were widened by edema and hemorrhage so that the follicles became widely separated. In still other areas there was appreciable fibrosis with atrophy of follicles; the fibrous tissue was cellular in some foci and partly hyalinized in others. Numerous hematoidin crystals were present in areas of recent hemorrhage. A few spicules of bone, some of them necrotic, were seen deep within the tumor.

Sections taken through rib and adjacent tumor showed invasion of the bone by tumor with replacement of the marrow by a loose connective tissue. There was active formation of new bone, usually by apposition on old trabeculae, together with a lesser degree of osseous destruction. Spicules of bone

Fig. 5.—Circled area in figure 7 slightly reduced from a low power magnification of 25 times. Note narrow zone of viable tumor around blood vessel (*b*) which showed uptake of radioactive iodine in figure 6.

were seen deep within the tumor itself; some of them were new bone arising from connective tissue septums. Similar new bone formation from connective tissue was seen in one place in the capsule.

The diagnosis was metastatic thyroid adenocarcinoma of the differentiated small follicle type.[15]

Subsequent Treatment and Course: From Jan. 23 to Feb. 21, 1944, the patient was submitted to a course of treatment with thiouracil. This was done to check further on the functional nature of the metastases. The thiouracil therapy produced a striking remission of the hyperthyroidism, which, however, promptly recurred after the treatment was discontinued. The effect of thiouracil on the objective criteria of hyperthyroidism is shown in figure 2.

By the end of April 1944 the patient's condition had reached what might be called a state of equilibrium. His weight remained unchanged for two months at the level of 48 Kg., with basal metabolic rate at about + 10 per cent and the

15. Dr. S. H. Rosen and Dr. David Marine.

plasma cholesterol level between 200 and 214 mg. per hundred cubic centimeters. The blood iodine on March 24 was 9.4 micrograms per hundred cubic centimeters. Roentgenograms taken on April 21, 1944, showed no detectable changes in the various metastases. The second therapeutic dose of radioactive iodine, 55.4 millicuries of the eight day isotope, was administered on April 28, 1944. Twenty-seven per cent of this dose (13.8 millicuries) was extracted from a twenty-one hour urine collection [16] and readministered on April 29. A second fraction from urine was obtained later (6.3 millicuries) and readministered on April 30. Thus a total of 75.5 millicuries was administered within three days, giving a radiation dose of 18,200 equivalent r to the tumor and 64 equivalent r to the blood. The white blood cell count showed only a slight temporary fall from 6,000 to 4,500, which, in our opinion, was not significant. The basal metabolic rate dropped to zero in about three weeks and remained at about this level until March 1945. The plasma cholesterol fluctuated from a level of about 200 mg. per hundred cubic centimeters to a somewhat higher level. The blood iodine level dropped to 6.5 micrograms on June 10, 1944, to 4.7 micrograms on Oct. 7, 1944 and to 5.1 micrograms per hundred cubic centimeters on Feb. 8, 1945. The patient's weight began to rise about three weeks after the administration of the therapeutic dose of radioactive iodine and continued to rise steadily from 48 Kg. in April 1944 to 53 Kg. in January 1945. Shortly after this second therapeutic dose of radioactive iodine a temporary sharply circumscribed alopecia appeared over the area corresponding to the skull metastasis. The patient's general well-being improved, his pains diminished, his locomotion improved, and he complained of getting fat. Roentgenograms on Aug. 19, 1944 and Feb. 6, 1945 showed no change.

From Feb. 8 to 25, 1945, the patient was given intramuscular injections of thyrotropic factor (Armour's; Rowlands-Parkes' units per cubic centimeter). The injections were given in divided doses every one or two days for a total of 33 cc. in eighteen days. During this interval of treatment there was no rise in the basal metabolic rate, no significant change in plasma cholesterol and a slight fall in blood iodine (from 5.1 to 4.1 micrograms per hundred cubic centimeters). Bioassays of the urine for thyrotropic hormone [17] both before and during the interval of this treatment were negative, indicating that the patient's own thyrotropic hormone was inactivated by the tumor tissue.[18]

On March 3, 1945, the third therapeutic dose of radioactive iodine was given. It consisted of 41.6 millicures of I^{131} plus 16.0 millicuries recovered from the urine and fed three days later. The total of 57.6 millicuries gave a tumor dose of 11,600 equivalent r, a blood dose of 41 equivalent r. The patient's weight increased and the basal metabolic rate, which was in the normal range immediately before the treatment, dropped to −27 per cent in about three months and has remained consistently low. The plasma cholesterol increased slightly and has remained above the pretreatment level. The blood iodine dropped from 4.1 micrograms per hundred cubic centimeters immediately before this third therapeutic dose to 0.8 microgram per hundred cubic centimeters three months later.

The patient's general condition is good. He moves freely about the hospital and is engaged in occupational therapy.

Fig. 6.—Radioautograph of an entire unstained section of metastatic tumor in second rib on the left side with magnification slightly reduced from 8 times, showing distribution of radioactive iodine in the viable tissue.

Fig. 7.—Photomicrograph of section used for figure 6 stained with eosin and hematoxylin, same magnification. Note viable (dark) and necrotic (light) areas.

Fig. 8.—photograph of figures 6 and 7 superimposed, showing coincidence of radioactive iodine distribution with the viable tumor.

COMMENT

Adenocarcinoma of the thyroid is generally considered highly radioresistant. H. F. Hare [19] specifically stated that alveolar carcinoma of the thyroid is not changed histologically by 6,000 r (x-ray). For a successfully treated patient (his case 2) Hare gives the dimensions of the tumor and the interstitial radon dose employed. Calculations show the gamma ray dose to be close to 20,000 r, a value well beyond the reach of external radiation.

16. Dr. E. J. Baumann, Chemistry Department, Montefiore Hospital, developed a procedure for extracting iodine from urine so that it could be refed to the patient in the form of sodium iodide. This technic was utilized whenever the amount of I^* involved warranted it. The efficiency of recovery was consistently high, 80 to 95 per cent.

17. Determinations were made on young guinea pigs weighing 200 Gm., using total weight of thyroid gland and degree of hyperplasia as criteria. Extraction of thyrotropic hormone from the urine followed the method described by Jones, M. S.: Study of Thyrotropic Hormone in Clinical States, Endocrinology **24**: 665-671 (May) 1939.

18. Seidlin, S. M.: The Metabolism of the Thyrotrophic and Gonadotrophic Hormones, Endocrinology **26**: 696-702 (April) 1940. Rawson, R. W.; Sterne, G. D., and Aub, J. C.: Physiological Reactions of the Thyroid-Stimulating Hormone of the Pituitary: I. Its Inactivation by Exposure to Thyroid Tissue in Vitro, ibid. **30**: 240-245 (Feb.) 1942.

19. Hare, H. F.: Radiation Treatment of Carcinoma of the Thyroid, Am. J. Roentgenol. **46**: 451-453 (Oct.) 1941.

Since 1 microcurie of 8 day iodine destroyed per gram of tissue gives approximately 150 equivalent r,[20] to achieve comparable dosage we must concentrate at least 133 microcuries in each cubic centimeter of tumor, if turnover is assumed to be zero. For our patient, with approximately 300 cc. of tumor tissue, such a dose would require that 40 millicures of I^{131} be fixed in the tumors. The actual amount to be fed, however, may be several times this amount, because of the loss of iodine by excretion and by deposition in other tissues, especially if normal thyroid tissue is present.

Fig. 9.—Higher magnification (400 times) of section taken at X in figure 7. Note follicular structure and colloid-like material (*c*) in a few follicles.

In addition to these rough quantitative considerations, criteria of a biologic nature, such as the time factor and lack of irradiation of the tumor bed beyond a few millimeters, must be considered in comparing the results of 8 day iodine beta ray therapy with those of 3.82 day radon gamma ray therapy. These remain to be assessed on the basis of additional experience.

Over a period of three years, our patient has received nearly 40,000 equivalent r to each of his tumors. In spite of the remarkable clinical improvement, it cannot be concluded that the functioning tumors have been completely destroyed because recent tracer studies, although showing a marked increase in excretion, still show localization of radioactive iodine in the lesions. Further therapy is indicated and is being planned, the limiting factor being the availability of the isotope in sufficient quantity. The criterion for completion of I * therapy will be the lack of radioactive iodine pickup by any of the known metastases, although the possibility remains that the tumors, even in the absence of any uptake, will not be completely destroyed.

20. A complete description of experimental methods and calculations will be given in a companion paper now in preparation.

All available roentgenograms taken of this patient since July 1939 were reviewed recently in order to evaluate as precisely as possible the progress of the various skeletal lesions. Between July and October of 1939, films were made of the spine, pelvis, skull, arms, legs and left femur. At this time all the regions were negative for metastases. In November 1939, the extraosseous metastatic tumor in the back was removed. By 1941 there were early lesions in the right femur, right ileum and chest as described in the case history. These lesions increased in size, and the one in the skull was discovered in 1943. Frequent plates were taken of all these regions from 1942 until the present, and they show that there was no increase in the area of bone destruction in any region after the first therapeutic dose of I * was administered in 1943. Representative films showing the progress of three of the lesions are shown in figures 10, 11 and 12.

The urinary excretion of radioactive iodine was followed after almost every dose, tracer or therapeutic; on several occasions the collection period was longer than a month. As an illustration, the data obtained after the dose of Aug. 5, 1943, is shown in figure 13. Plotted on semilogarithmic paper, the curve shows two distinct, consecutive rates of change in daily excretion, the break occurring three days after administration. In the same figure a second curve is shown which represents the daily excretion of radioactive iodine by this patient soon after the cessation of thiouracil therapy. The data as a whole seem consistent with the hypothesis that in both instances the excretion of radioactive iodine within three days of administration is governed by a mechanism different from the one which governs its excretion thereafter.

The concentration of radioactive iodine in the blood as a function of time was studied in order to gain information of physiologic and radiologic significance. Shown in figure 14 is a composite curve obtained after the administration of the last two therapeutic doses of radioactive iodine (April 28, 1944; March 3, 1945). The individual determinations pertaining to each study are shown in detail. The data of Frantz and her associates[4] are also shown for comparison. From the curve it is seen that the level of I * in the blood

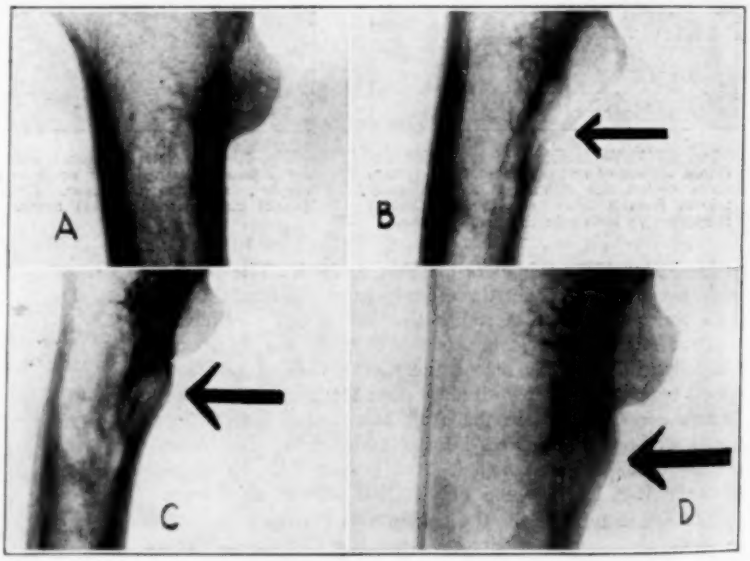

Fig. 10.—Roentgenologic appearance of lesion of the femur on *A*, Oct. 30, 1939; *B*, Oct. 29, 1942; *C*, June 22, 1944, and *D* (a higher magnification), May 22, 1946.

remains essentially constant for a considerable period after the first day. An analysis of the detailed data obtained on this particular patient indicates that the curve represents three different phases; a rapid initial turnover (about twenty-four hours) which is succeeded by a stabilized level of one week's duration, and finally, a slow but steady decline.

Many authors have reported significant drops in the white blood count after the administration of radioactive isotopes other than iodine. Our experience with large doses of radioactive iodine shows that with this element the effects on the white blood cells are not pronounced and are short-lived. A drop in total leukocytes with no significant variation in the differential was observed after the administration of large amounts of I^{130} but not after the use of I^{131}, although the total blood dosages were comparable in magnitude. However, since radiation from the 12.6 hour isotope is delivered almost entirely within two days, whereas from the 8 day isotope nearly the same proportion is delivered within thirty-two days, we must infer that the time factor is mainly responsible for the previously stated results. This is analogous to many other radiobiologic phenomena such as erythema production with single and fractional roentgen therapy, in which time is an important factor.

It is logical to assume that the effect of this factor on tumor tissue will be in the same direction as it is on the blood. Therefore, consideration of the time factor alone might seem to contraindicate the use of I^{131} in the treatment of tumors because higher doses would be required to obtain a given effect. The value of radiation treatment, however, must be based on the differential effect on both tumor and normal tissue. It can be shown for oral administration of the isotope that the ratio of the tumor dose [21] to the blood dose is about 80 when I^{130} is used and about 300 when I^{131} is used. Thus, the use of I^{131} would be approximately four times as effective as the use of I^{130} if there were no time factor involved. To offset this advantage the differential time factor would have to render the 12.6 hour isotope more than four times as effective for a given blood dose as the 8 day isotope before there could be a question about the advisability of the use of I^{131} in preference to I^{130}. This remains to be determined.

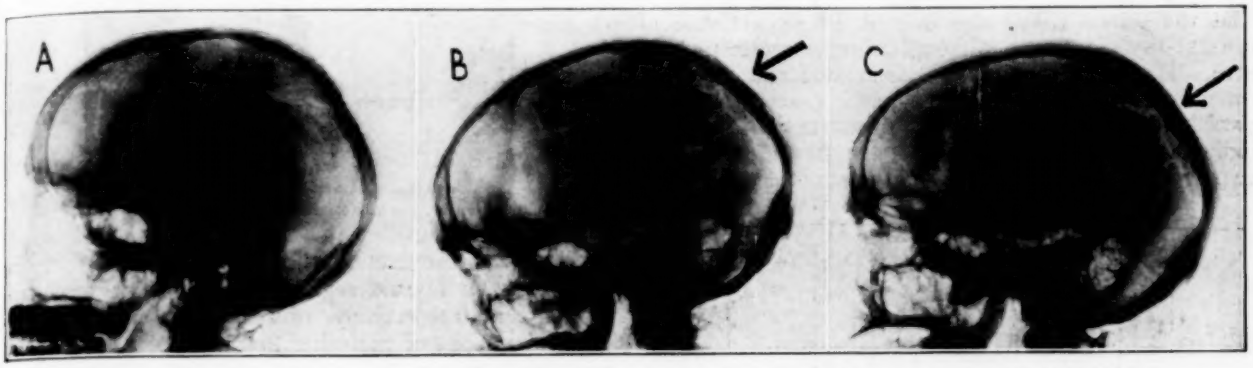

Fig. 11.—Roentgenologic appearance of lesion of the skull on *A*, Oct. 30, 1939; *B*, May 18, 1943, and *C*, Feb. 4, 1946.

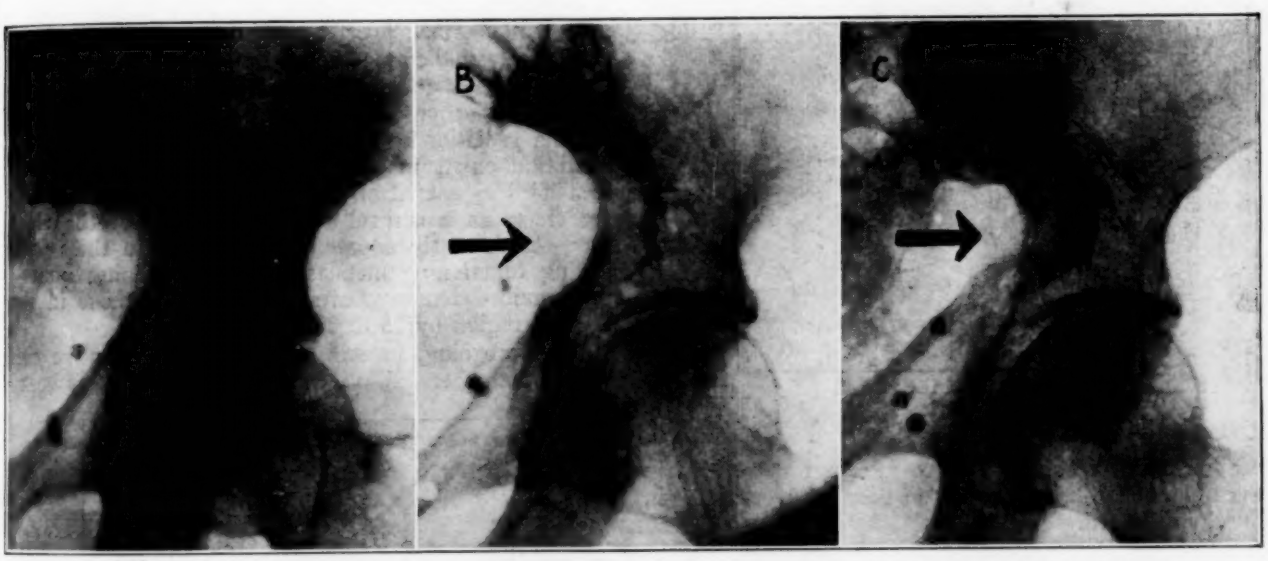

Fig. 12.—Roentgenologic appearance of lesion of ilium on *A*, July 17, 1939; *B*, Nov. 10, 1942, and *C*, May 22, 1946.

In earlier studies [22] of thyroid–iodine metabolism by the use of I^* it was shown that irrespective of the total amount of iodine administered, the hyperactive gland initially retains more I^* than the normal gland but loses it faster. The rate of loss seems to increase with larger amounts of carrier iodine.

With this in mind as well as with the purpose of determining ultimately the actual radiation dose deliv-

21. Calculated on the basis of the experimental curve of concentration of the I^* in the blood and a net tumor elimination rate of 0.5 per cent per day.

22. Hertz, S.; Roberts, A., and Salter, W. T.: Radioactive Iodine as an Indicator in Thyroid Physiology: IV. The Metabolism of Iodine in Graves' Disease, J. Clin. Investigation **21**: 25-32 (Jan.) 1942. Hamilton.[3]

ered to the tumors, the I * turnover in the lesions was studied by means of suitable Geiger-Mueller counters under reproducible geometric conditions. This was done several times between May and August 1943, as well as ten months and one year after the third therapeutic dose. Unfortunately, the 1943 measurements—due to circumstances partially beyond our control—cannot be interpreted without making some assumptions. The only thing that can be said is that several days after the administration of a tracer dose of I^{131} the activity of all the lesions, when corrected for decay of 8 day iodine, disclosed the elimination of about 0.5 per cent of the dose per day. This observation per se cannot be interpreted as a demonstration that the tumor tissue metabolized I * at the rate of normal thyroid tissue, although this was our impression. The latest data (1946), figures 15 and 16, taken much more accurately, show a rapid loss of I * in the two lesions studied when 40 micrograms of carrier iodine was administered. With the larger amount of carrier iodine, the rate of loss was not as great, in

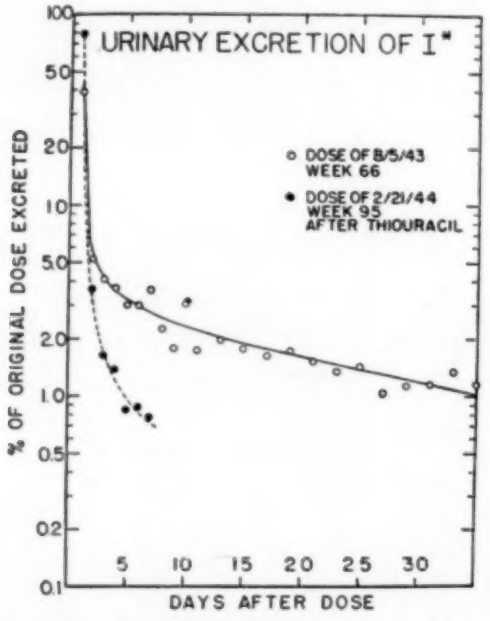
URINARY EXCRETION OF I*
% OF ORIGINAL DOSE EXCRETED
DOSE OF 8/5/43 WEEK 66
DOSE OF 2/21/44 WEEK 95 AFTER THIOURACIL
DAYS AFTER DOSE

Fig. 13.—Typical trend of urinary excretion of I *.

proportion. We are unable to interpret these data in the light of published works on the turnover of I * in the thyroid itself.

Owing to the unusual nature of this case, that is, hyperthyroidism despite total thyroidectomy, the procedure and results of our studies of radioactivity over the region of the original thyroid as well as over the metastases may be of interest.

The experimental setup and the theoretic considerations will be described in detail in another paper. It suffices to state here that the Geiger counter is shielded with a ¾ inch (1.91 cm.) thickness of lead and provided with a suitable window. The activity of any lesion or region is obtained by taking the difference between readings with the window open and those with the window plugged with a ¾ inch (1.91 cm.) thickness of lead. This method greatly facilitates the localization of radioactive iodine in contiguous lesions.

The counter readings over the thyroid area were on the average only 5 per cent of the readings obtained over the metastasis of the skull. This percentage did not change materially throughout the course of the study. The readings over the thyroid region were two to three times the readings taken over the lateral surface of the right calf but consistently less than readings obtained over the apex of the right lung, although both regions were free from metastases. A comparison with 2 nonthyroidectomized patients under similar conditions

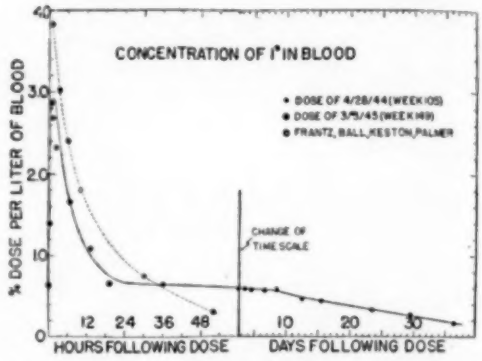
CONCENTRATION OF I* IN BLOOD
% DOSE PER LITER OF BLOOD
DOSE OF 4/28/44 (WEEK 105)
DOSE OF 3/5/45 (WEEK 149)
FRANTZ, BALL, KESTON, PALMER
CHANGE OF TIME SCALE
HOURS FOLLOWING DOSE
DAYS FOLLOWING DOSE

Fig. 14.—Concentration of I * in the blood (corrected for decay) after oral administration of the radioactive element.

of dosage and excretion showed that iodine pickup in this patient's thyroid region was only 4 per cent and 6 per cent, respectively, of the iodine pickup in the thyroid regions of the other 2 patients.

While the evidence presented herein shows clearly that there was little activity over the thyroid region, it might be argued that since this activity was greater than that obtained over the calf, the existence of some residual thyroid tissue cannot be ruled out. However, the presence of functioning metastases in the neighborhood of the thyroid region will cause some scattered gamma radiation to enter the instrument. No similar condition exists in the region of the calf, which was first used as a control. But when, with this in mind, we chose as a control region the apex of the right lung—analogously situated with respect to the neighboring functioning metastases, but containing none—we obtained readings even greater than those in the thyroid region by 15 to 30 per cent.

The foregoing, in our opinion, is presumptive evidence that there is no functioning thyroid tissue in

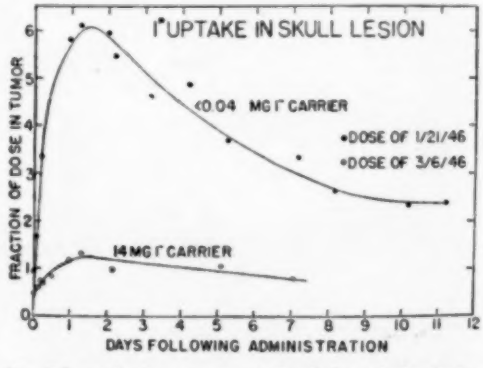

Fig. 15.—I * uptake in a representative lesion of the skull subsequent to the administration of doses containing different amounts of carrier iodine.

the neck and confirms the previous surgical observations.

It is pertinent to mention that 4 cases of metastatic carcinoma of the thyroid without clinical hyperthyroidism have been studied with radioactive iodine and have shown selective localization in the lesions. Two of these are now under treatment with I.*

SUMMARY

A case of metastatic adenocarcinoma of the thyroid is reported in which treatment by means of radioactive iodine has been successful. The patient was completely thyroidectomized for "malignant adenoma" in 1923, with neither thyrotoxicosis then nor hypothyroidism postoperatively; fifteen years later there developed classic symptoms of hyperthyroidism and severe pain in the lower back. In October 1939 a pulsating tumor removed from the level of the twelfth thoracic vertebra proved to be metastatic thyroid adenocarcinoma (histologically well differentiated, with small follicles and colloid). In the next two years hyperthyroidism increased and roentgenograms revealed new metastases in the lungs, upper part of the right femur, second rib on the left side, left ileum and skull. Roentgenologic irradiation of the metastases proved ineffectual.

In March 1943 a tracer dose of radioactive iodine revealed iodine retention by all the known lesions and no evidence of residual thyroid tissue in the neck. Therapeutic amounts of radioactive iodine were administered orally between May and October 1943. Definite and lasting clinical improvement followed. In April 1944 and March 1945 additional I * was administered with a resultant disappearance of pain, increase in weight and progressive change in all clinical criteria in the direction of hypothyroidism. Roentgenographic evidence pointed to an arrest if not a regression of the disease. No untoward effects followed this therapy.

Radioactive iodine seems to be an effective therapeutic agent in the control of this type of tumor.

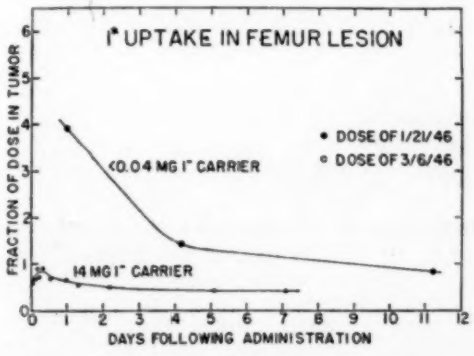

Fig. 16.—I * uptake in a representative lesion of the femur subsequent to the administration of doses containing different amounts of carrier iodine. The fraction of dose in the tumor is proportional to the ratio of counts obtained over the given lesion under fixed geometric conditions to counts obtained at the same time on an aliquot part of the administered I *. Thus, figures 15 and 16 represent correctly the time change in concentration in any one lesion, but because of the geometric differences involved in the measurements they do not permit direct comparison of the I * concentration in the two lesions.

Fundamental Research and the Rh Factor.—The fundamental basis for the recognition of the Rh factor was laid in 1900 when three important discoveries were made. First, the mendelian laws of heredity, published thirty-five years previously, were independently rediscovered by Correns, Tchermak and de Vries. Second, in the same year Landsteiner discovered the phenomenon of normal isoagglutination as the basis of the four blood groups, and in the next year he mentioned their significance in the selection of donors for transfusion. Third, and of more immediate importance, Ehrlich and Morgenroth discovered the phenomenon of isoimmunization, which they demonstrated in goat blood and which other workers later demonstrated in many species.—Levine, Philip, M.D.: The Present Status of the Rh Factor, *Am. J. Clin. Path.* October 1946.

TREATMENT OF EARLY SYPHILIS WITH CALCIUM PENICILLIN-OIL-BEESWAX

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and
CHARLES R. REIN, M.D.
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Washington, D. C.

The early development and progress in the production of a suspension of calcium penicillin in beeswax and peanut oil has already been reported.[1] The initial successful clinical results in the treatment of gonorrhea [1c] by a single injection of this mixture suggested its use for the treatment of syphilis. It should be emphasized that the primary purpose of this paper is to illustrate an ambulatory method of therapy whereby the patient receives one injection of penicillin instead of the usual eight injections a day.

This study was initiated in August 1944. Since then 75 patients with early syphilis have been treated, of whom 72 were men and 3 women. The ages varied from 18 to 44. There were 37 white and 38 Negro patients. Fifty-six had primary syphilis, of whom only 6 were seronegative, while the remaining 19 had secondary syphilis. All patients were subjected to serologic examination prior to institution of treatment. Dark field examinations gave positive results in 73 patients. The remaining 2 gave a history of having had a penile lesion followed by the development of a generalized eruption and had persistent strongly positive serologic reactions for syphilis, but dark field examinations were not made. Before treatment 31 patients with primary syphilis and 16 with secondary syphilis had an examination of the spinal fluid, which included cell count, Kolmer complement fixation, total protein, globulin and colloidal gold tests. The 31 patients with primary syphilis had normal spinal fluids, while 4 of the 16 with secondary syphilis had abnormal spinal fluids.

The treatment consisted of the daily intramuscular (buttock, deltoid or triceps) administration of 300,000 units of calcium penicillin in beeswax and peanut oil for eight days.

Of the first 14 patients treated, 2 received 100,000 units three times a day, 2 received 150,000 units twice a day and 10 received 300,000 units in 2 or 3 cc. once a day. The remaining 61 patients received 300,000 units in 1 cc. The total number of Oxford units for all patients was 2,400,000 which is comparable to the

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From the Penicillin Section and Medical Service, Walter Reed General Hospital, and the Department of Serology, Army Medical School, Army Medical Center (Mr. Rittman).

Major Romansky is now civilian consultant in antibiotics to the office of the Surgeon General, U. S. Army, and associate clinical professor of medicine, George Washington University School of Medicine, Washington, D. C.

Assistance was rendered by the following medical officers: Captain Robert J. Murphy, Captain Aubrey Harwell, Captain Samuel Katz, Captain Francis W. Epstein and Captain Merritt E. Roberts. Miss Mina Levy, Miss Dorothy Talbott, Miss Jewel Patton, Miss Lillian Axelrod, Miss Sarah McDearman and Sergeant Leslie H. Wood gave technical assistance.

1. (*a*) Romansky, M. J., and Rittman, G. E.: Method of Prolonging Action of Penicillin, Science **100:** 196, 1944; (*b*) Penicillin: Prolonged Action in Beeswax-Peanut Oil Mixture; Single Injection Treatment of Gonorrhea, Bull. U. S. Army M. Dept., no. 81, p. 43, 1944. (*c*) Romansky, M. J.; Murphy, R. J., and Rittman, G. E.: Single Injection Treatment of Gonorrhea with Penicillin in Beeswax-Peanut Oil: Results in One Hundred and Seventy-Five Cases, J. A. M. A. **128:** 404 (June 9) 1945.

practice of giving sixty injections in seven and one-half days for the same total.

The schedules of therapy for the first 14 patients were necessary since the potency of the then available calcium penicillin was inadequate to produce a mixture which would maintain satisfactory levels in the blood for approximately twenty-four hours after a single intramuscular injection. As soon as calcium penicillin with a potency of approximately 1,000 units per milligram was available, it was possible to suspend 300,000 units in 4.8 per cent beeswax (by weight) in peanut oil contained in 1 cc. As shown in a previous report,[2] this mixture will maintain satisfactory assayable levels in the blood for about twenty to twenty-four hours after a single injection and continue to be excreted in the urine for about three days. Patients 15 to 75, therefore, received the preparation consisting of 300,000 units of calcium penicillin in 4.8 per cent beeswax in peanut oil contained in 1 cc.

Blood was obtained at thirty minutes and at four hour intervals for twenty-four hours in order to determine the penicillin levels. During the subsequent seven days of therapy, blood was withdrawn at the twenty-fourth hour after injection for the same purpose. Specimens of urine were obtained for six days following the last injection in order to determine for how long a period penicillin continued to be excreted. Dark field examinations were repeated at frequent intervals in order to determine the disappearance time of the spirochetes. Patients were also observed for the appearance of Herxheimer reactions. Daily inspections were made to determine the time of healing of syphilitic lesions. The patients were observed for a minimum of fifteen days, during which time additional specimens of blood were withdrawn for serologic examination. Blood was also withdrawn monthly for as long as possible. Each serum was subjected to a battery of six qualitative serodiagnostic procedures, including Kline diagnostic, Kline exclusion, Mazzini, Kahn and Kolmer tests as well as a new microflocculation test employing a cardiolipin antigen.[3] All serums which gave a four plus reaction with any of the foregoing procedures were also tested quantitatively by the same procedures.

Results of 75 Cases of Early Syphilis Treated by a Single Daily Intramuscular Injection of 300,000 Units of Calcium Penicillin in 4.8 Per Cent Beeswax in Peanut Oil Contained in 1 Cc. for Eight Days

Length of Time Followed, Mo.	Attained Seronegativity		Satisfactory Clinical and Serologic Follow-Up			
	Primary Syphilis	Secondary Syphilis	Primary Syphilis	Secondary Syphilis	Relapse, Secondary Syphilis	Not Followed
Less than 3..	6	..	2	3	..	15
3.....	5	..	4	1	1	..
6.....	7	..	3	1	1	..
9.....	7	2	..	2	..	..
12 or more...	12	1	..	2	..	..
Total cases	37	3	9	9	2	15

Penicillin was continuously present in the blood during the eight days of therapy. Its presence in the urine for six days following the last injection indicated that penicillin was present in the blood for a total of fourteen days. When penicillin in aqueous solution is administered in sixty intramuscular injections of 40,000 units every three hours for seven and one-half days, penicillin will not be present in the blood at the end of the eighth day. This indicates that with the same total dosage (2,400,000 units) patients receiving the beeswax and peanut oil mixture may have the benefit of penicillin for an average of five to six days more than those who receive sixty injections of the aqueous solution.

The lesions were rendered dark field negative in ten to thirty-six hours after the initial injections of penicillin in beeswax and peanut oil. Fifty-two per cent were negative by the twelfth hour, 97 per cent by the twenty-fourth hour and the rest by the thirty-sixth hour.

In 39 per cent of the patients some degree of Herxheimer reaction developed, as evidenced by a slight to moderate rise in temperature. Ten per cent of these also had a concomitant cutaneous reaction, as manifested by exacerbation of an existing secondary eruption or the development of a rash.

Both primary and secondary lesions were healed in three to twelve days, with an average healing time of seven days.

Of the 75 patients treated, results for 60 are shown in the table. The remaining 15 patients could not be followed clinically or serologically for a sufficient length of time to be evaluated. These patients, however, are included, since they showed a satisfactory time for disappearance of the spirochetes and a rapid healing of primary and secondary syphilitic lesions. Forty (66.6 per cent) of the 60 patients attained and maintained seronegativity with all tests in the serologic battery for the period of follow-up. An additional 18 patients (30.0 per cent) showed satisfactory progress at the time of the last serologic examination. There was, therefore, a satisfactory response in 58 of the 60 patients followed. The results in 2 patients (3.3 per cent) with secondary syphilis are classified as failures. There were two reinfections. Both of the patients with reinfection had attained and maintained seronegativity following treatment. Thereafter, a new seronegative dark field–positive primary lesion developed. Serologic reactions subsequently became positive. Contacts with infectious syphilis were established in both instances.

Of the 40 patients who attained seronegativity, 37 had primary and 3 had secondary syphilis. It is interesting to note that all patients who became seronegative within six months had primary syphilis, whereas the 4 patients who were still seropositive (but had shown a satisfactory response) at nine or more months following therapy had secondary syphilis.

Some of the factors which determined the length of time required to attain seronegativity are as follows: (1) the stage of the disease at the time treatment was instituted (examinations of patients with primary syphilis gave negative results earlier than those of patients with secondary syphilis); (2) the serologic titer at the onset of treatment (examinations of patients with low-titered serologic reactions gave negative results earlier than those of patients with high-titered serologic

2. Romansky, M. J., and Rittman, G. E.: Penicillin Blood Levels for Twenty-Four Hours Following a Single Intramuscular Injection of Calcium Penicillin in Beeswax and Peanut Oil, New England J. Med. **233**: 577, 1945.

3. Rein, C. R., and Bossack, H. N.: Cardiolipin Antigens in the Serodiagnosis of Syphilis: A Microflocculation Slide Test, Am. J. Syph., Gonor. & Ven. Dis. **30**: 40, 1946.

reactions), and (3) sensitivity of the tests employed (tests with greater sensitivity maintained seropositivity for longer periods than did the less sensitive tests).

It is important that all patients receiving penicillin therapy be subjected to serologic examinations at frequent intervals (at least once a month) in order to detect serologic relapse and impending clinical relapse as early as possible. A serologic relapse usually precedes a clinical relapse by about one month.

Twenty-four hours after the intramuscular injection of penicillin in beeswax and peanut oil there was some soreness to pressure at the site. This was usually gone by the forty-eighth to seventy-second hour. This sequence of events occurred after each injection, although the injection was administered at a different site. The soreness was no severer than that following the multiple injections of an aqueous solution of penicillin, and the patient had the added advantages of being on an ambulatory basis and of receiving only one injection a day. It is not desirable to massage the site of injection, since diffusion of the material will accelerate absorption and increase local soreness.

Studies of tissue in animals and in human beings [4] from the sites of injection of calcium penicillin in beeswax and peanut oil show that, although the material may be injected subcutaneously, considerably less reaction occurs when it is given intramuscularly. Clinically, this is also true, as indicated by subjective and objective findings.[4a] This has also been corroborated by Nichols and Hauntz [5] but it is contrary to the report of Kirby and associates,[6] who stated that less discomfort occurs following the subcutaneous administration of penicillin in beeswax and peanut oil.

Two patients in this group had allergic reactions manifested by the development of urticaria five to six days following the eighth injection. The urticaria was similar to that seen after the use of an aqueous solution of penicillin and lasted for six to seven days, reaching its peak on the fourth day. The incidence of allergic reactions after the intramuscular use of calcium penicillin in beeswax and peanut oil is about the same as that following the use of an aqueous solution of penicillin by multiple injections or by other routes. Reactions at the site of injection are more frequent when penicillin in beeswax and peanut oil is given subcutaneously. The preceding conclusion is based on the treatment and study of approximately 500 patients given a single daily injection of calcium penicillin in beeswax and peanut oil for a variety of diseases.[4] No other untoward reactions were noted as a result of the administration of this mixture. Beta-dimethylaminoethyl benzhydryl ether hydrochloride (Benadryl), a new drug, is effective in most instances in alleviating the allergic manifestations produced by penicillin. We have also used it simultaneously with penicillin to prevent the allergic complications in patients who have previously been sensitive to penicillin.

The present preparations of calcium penicillin in beeswax and peanut oil present no difficulty in administration, since they can be administered with a 22 gage needle at room temperature (25 C.) if necessary. However, the practical needle for routine use is the 20 gage. This is best illustrated by the fact that over fifty thousand injections of this preparation have been given by the nursing staff at the Walter Reed General Hospital in the treatment of all conditions necessitating the use of penicillin. In the early preparations some trouble in withdrawal and administration was experienced. As a rule this was due to the occasional difficulty in properly blending the penicillin powder, with the result that the mixture was viscous and occasionally large particles obstructed the passage of the mixture through the needle. The method of administration has been reported previously.[2] However, one point should be emphasized. Once the material is drawn into the Luer-Locke syringe it should be allowed to cool to room temperature prior to injection. It is unnecessary to rewarm the syringe. In view of its stability, the calcium penicillin in beeswax and peanut oil can be kept at room temperature for at least a year.[7]

It has been stated previously [8] that because of the hygroscopic factor in the noncrystalline sodium salt the calcium salt must be used in the preparation of penicillin in beeswax and peanut oil mixtures. This is contrary to a recent report of Leifer and Kirby [9] who stated that the sodium salt may be used as well as the calcium. It has been observed that not only does the noncrystalline sodium salt produce erratic and less prolonged levels than the calcium but, more important, it does not maintain its stability.[10] Furthermore, there is a tendency for the particles of sodium salt to congeal into clumps in the beeswax and peanut oil mixture, preventing passage of the material through the needle. These difficulties may be obviated when crystalline sodium salt is available for the preparation of the penicillin-beeswax-peanut oil mixture.

The data presented indicate that early syphilis may be treated by the described ambulatory method, only one daily injection of penicillin being employed for eight days. We, as well as others, have encountered failures regardless of the penicillin schedule used. With the hope of reducing the number of such failures, we have initiated a study in which the same single dose of 300,000 units of penicillin is administered daily over a period of sixteen days for a total of 4,800,000 units. An additional group of patients with early syphilis is being treated on the same schedule with crystalline penicillin G in beeswax and peanut oil.

SUMMARY

1. An ambulatory method for the treatment of early syphilis is described. A single daily intramuscular injection of 300,000 units of calcium penicillin in 4.8 per cent beeswax in peanut oil contained in 1 cc. is administered for eight days.

2. Fifty-eight of the 60 patients thus treated and followed gave satisfactory results. Although the number of patients in this study is too small to be statistically significant, the results obtained with this method of therapy suggest a favorable trend.

4. (*a*) Romansky, M. J.: The Current Status of Calcium Penicillin in Beeswax and Peanut Oil: Data from a Study of 600 Cases and Clinical Observations of 4,000 Patients Given 60,000 Injections, Am. J. Med. **1**: 395, 1946. (*b*) Romansky.[3a,b]

5. Nichols, D. R., and Hauntz, C. A.: Prolonged Action of Penicillin in Mixtures of Beeswax and Peanut Oil, Proc. Staff Meet., Mayo Clin. **20**: 403, 1945.

6. Kirby, W. M. M.; Martin, S. P.; Leifer, W., and Kinsman, J. M.: Maintenance of Therapeutic Blood Concentrations of Penicillin for Twenty-Four Hours Following Single Injections of Penicillin-Beeswax-Peanut Oil Mixtures, J. Lab. & Clin. Med. **31**: 313, 1946.

7. Romansky, M. J.: The Stability of Non-Crystalline Calcium Penicillin in Beeswax and Peanut Oil at 10°, 25°, 37°, 56° and 100° C., to be published. Romansky.[4]

8. Footnotes 1 and 2.

9. Leifer, W., and Kirby, W. M. M.: The Treatment of Gonococcal Urethritis with Single Injections of Penicillin-Beeswax-Peanut Oil Mixtures, New England J. Med. **233**: 583, 1945.

10. Footnotes 1, 4 and 7.

ABSTRACT OF DISCUSSION

Dr. Donald R. Nichols, Rochester, Minn.: Mixtures of beeswax and peanut oil have been used successfully to prolong the action of several drugs. Romansky and his colleagues have reported in detail their method of prolonging the action of calcium penicillin by suspending it in a mixture of beeswax and peanut oil. At the request of the Office of the Surgeon General of the United States Army, Herrell and I undertook to evaluate this method of administration. We previously had studied the calcium salt of penicillin and had found it generally satisfactory for intravenous and intramuscular treatment of bacterial infections and no more irritating to tissues than the sodium salt. The suspension of calcium penicillin in beeswax-peanut oil mixtures was found to be a practical and effective method of delaying the absorption of penicillin after intramuscular and subcutaneous administration. A concentration of at least 0.03 of an Oxford unit of penicillin was maintained in the blood for twenty-four hours following a single intramuscular injection of 300,000 units of calcium penicillin in a 4.8 per cent mixture of beeswax and peanut oil. Previously the viscosity of the mixture made the administration of this preparation difficult. However, suitable amounts are now dispensed in individual syringes so that a single dose can be injected directly into the tissues. This greatly lessens the difficulty of administration. The incidence of troublesome local reactions and generalized allergic reactions from penicillin in beeswax-peanut oil mixtures has been higher in our experience than that reported by Romansky. However, these reactions have been transient. There has been no evidence of any permanent foreign body reaction. The absence of any serious irritating effects and the convenience of huge concentrated doses which need be given only at relatively long intervals are factors which emphasize the practicability of this method of administration. It seems highly probable that penicillin administered in beeswax-peanut oil mixtures will be of value in the treatment of syphilis.

Dr. George V. Kulchar, San Francisco: Drs. Romansky and Rein have given a satisfactory, safe, ambulatory, effective method for the treatment of syphilis. It seems that this method has certain advantages over the use of sodium penicillin in aqueous solution. For one thing, I believe that the effect of the penicillin, as pointed out, is prolonged over fourteen days on the average, or six days longer than the ordinary course of sodium penicillin. The second advantage is the ease of administration. The fact that it does not require hospitalization is a great economic advantage. It however appears that there are certain disadvantages to this method. One is the higher incidence of reactions, about which Dr. Nichols spoke. In his series at Stanford University, Dr. Barnett informs me that with use of sodium penicillin in 200 cases there have been no reactions. The patients have been carefully scrutinized, so that I doubt much if any kind of reactions have been missed. At the San Francisco City Clinic, calcium penicillin in peanut oil and beeswax has been used for the last ten months. Dr. Koch, the director of venereal disease, has supplied me with the data from that series. Among 126 patients, 98 of whom completed treatment, there were 9 who had severe urticarial reactions. There are, I believe, several possible explanations for this higher incidence of reactions. Possibly calcium penicillin may act as an antigen to a greater extent than sodium penicillin. It may be that either the beeswax or the peanut oil—we know that peanut oil is an antigen—may serve to sensitize the patient. The more logical explanation is that the sensitization develops over a period of, say, nine to ten days. With a residue remaining in the buttocks over that period, it is possible that this may lead to sensitization. It would be interesting if a statistical study were made as to the actual time of appearance of reactions. In the series from the San Francisco City Clinic mentioned, there were 98 patients who are available for statistical analysis. The system that was used there consisted of administration of 150,000 units of penicillin in beeswax and peanut oil twice a day over a period of ten days. Of the 98 who are available for analysis, 27 have been observed from five to ten months. There were no clinical relapses; there were 11 per cent failures, based on the serologic reactions, practically the same criteria being used as those used by Drs. Romansky and Rein. There were no local reactions of any consequence, but 3.3 per cent of the patients had to stop treatment because of urticarial reactions. It is possible that with the use of Benadryl or the newer Pyribenzamine (N'pyridil-N'benzyl-N-dimethylethylenediamine) these reactions may be controlled.

Dr. Thomas H. Sternberg, Los Angeles: I congratulate Dr. Romansky on this paper and on the amount of work he put into the development of calcium penicillin in beeswax-peanut oil. He has made a valuable contribution to the entire field of chemotherapy. Shortly after Dr. Romansky began the treatment of his present series of patients, the Surgeon General authorized two additional centers for the purpose of studying this method of therapy. The first was located at Fort Bragg, N. C., under the direction of Major William Leifer, and the second at Camp Howze, Texas, and later at Camp Livingston, La., under the direction of Major Franklyn Grauer. These centers began to operate early in 1945 but were closed shortly after V-J day because of the rapid loss of patients coincident to demobilization. A total of 200 patients with early syphilis were treated, the schedule consisting of a single injection of 300,000 units of calcium penicillin in beeswax-peanut oil daily for eight days, for a total dosage of 2,400,000 units. The Romansky formula was used. Thirty-five of these patients were lost from observation immediately. The rest were followed four to ten months, a period so inadequate that conclusions cannot be drawn. Nevertheless, in 97 of the group the serologic reaction for syphilis was negative at the time of the last examination. Included in this group of 97 patients were 50 with seronegative primary, 31 with seropositive primary and 16 with secondary syphilis. The status of 62 patients was considered problematic, since the reagin titer was declining but the serologic reaction was still positive. There were six frank serologic or clinical relapses. In the summary of these data, it appears that the results are comparable to those that might be expected for the same period of follow-up with use of 40,000 units of sodium penicillin every three hours for sixty doses, for a total of 2,400,000 units. Penicillin blood levels following a single injection of 300,000 units of the penicillin-beeswax-peanut oil preparation (Romansky formula) were performed at Fort Bragg, N. C., by Kirby and Rammelkamp. They were unable to demonstrate penicillin in the blood for more than twelve to eighteen hours in the majority of patients. For this reason it is believed that a more adequate dosage, such as 600,000 units daily, either as a single or as a split injection, should be used in the ambulatory treatment of early syphilis.

Dr. Marion B. Sulzberger, New York: I, too, want to express admiration for the work reported here. I second the opinions of those who said that the reactions produced by this preparation are higher in incidence and perhaps somewhat different in character from those produced by the injections of aqueous solutions of penicillin or of penicillin in oil. My associates and I have seen a number of cases of local reaction at and around the site of injection of the penicillin and beeswax and oil which took the form of swellings with considerable redness. Some of these looked as though they were going to be large sterile abscesses. However, though disagreeable and uncomfortable, these lesions did not break down. None of the reactions we saw produced any serious or lasting consequences to the patient, but they did interfere with the use of this preparation. I think that Dr. Romansky and co-workers have brought us another, and extremely important, application of a well known, established principle of chemotherapy. It is my conviction that this penicillin suspension contrasts in effects with the penicillin solution in the same way as suspensions of bismuth preparations in oil contrast with the soluble salts of bismuth. Again, the same principle is involved when one administers epinephrine in oil and gets the prolonged effects which are not possible when epinephrine is administered in aqueous solution. Again, the same principle is used when one makes suspensions of antigens or allergens in oil or other mediums and thus tremendously increases or potentiates their immunologic effects. Landsteiner and Chase and their co-workers and particularly

Jules Freund have shown that one can take poorly antigenic or allergenic substances, such as tuberculin, and by suspending them in oily emulsions—for example, suspending tubercle bacilli in oily emulsions—can produce specific tuberculin sensitivity in laboratory animals. No such regular production of tuberculin sensitivity was possible before without an actual infection with living bacilli. I think that, as Dr. Kulchar said, it is not astonishing but is rather to be expected that this oil-wax suspension of penicillin should potentiate the antigenicity or allergenicity of penicillin and thus tend to produce a higher incidence of allergic reactions. Both beeswax and peanut oil are unknown, not chemically defined, substances, or rather mixtures, and it is impossible to maintain their constancy. Beeswax is a variable mixture of a good many different things, and beeswaxes are of many different qualities. They contain extractives from different kinds of flowers and plants, according to where the bees feed. American beeswax sometimes contains sufficient ragweed allergen, sufficient "oleoresins" of ragweed, to give positive reactions to patch tests in ragweed-sensitive persons. Peanut oils are variable natural products or mixtures. I don't think this is a serious criticism of this mixture of substances, but it is a consideration which should impel the search for other simpler substitutes which might have the same or even better effects.

DRS. ALFRED COHN, THEODORE ROSENTHAL and ISAAK GRUNSTEIN, New York: This report of favorable results in treatment of early syphilitic patients with calcium penicillin in beeswax and peanut oil may help to open the road for penicillin therapy of ambulatory patients with syphilis. Using a different oily vehicle—sodium penicillin in water in oil emulsion—the Venereal Disease Research Unit of the New York City Department of Health initiated a study on the treatment of early syphilis in March 1945, and it is still in progress and essentially in the experimental stage. However, the results obtained thus far justify a short discussion. A total of 35 male patients with early syphilitic infections received daily injections of penicillin in water in oil emulsions over a period of five days. The daily dose ranged from 400,000 to 1,000,000 Oxford units of penicillin administered intramuscularly at either twelve or twenty-four hour intervals. After total dosages of 2,000,000 to 5,000,000 Oxford units respectively, definite clinical regression of the syphilitic lesions was observed among all patients at the end of active therapy. Titrated Wassermann tests and flocculation tests (Kahn, Kline and Mazzini) were done on the serum of each patient before treatment and were repeated each time the patient reported for reexamination. As a rule the positive Wassermann reaction reversed to negative within a period of five to twenty-eight weeks. Of the 35 cases, 10 were followed for a varying period up to six months and 15 for a period of seven to twelve months, while 10 cases had no adequate follow-up. The only clinical relapse observed thus far occurred sixty days after treatment. This patient suffered from seropositive primary syphilis and was treated over a period of five days with a total dosage of 4,200,000 Oxford units of penicillin. Among the 15 patients remaining under observation for a period from seven to twelve months, none showed any signs of a clinical relapse. The serums of 2 patients yielded gradually decreasing positive reactions to the complement fixation and flocculation tests over a prolonged period of eight to ten months. In a third patient with secondary syphilis the serologic reaction reversed from negative to positive eight months after treatment. Intramuscular injections of penicillin in water in oil emulsion did not produce any serious local or systemic effects except transitory pains at the site of injection. Herxheimer reactions of a mild degree occurred in most cases. . . . These findings corroborate also the observations of Jawetz, who demonstrated in experiments on animals that the action of penicillin apparently persists after disappearance of the drug from the blood stream.

DR. G. W. BINKLEY, Cleveland: My associate, Dr. Johnson, and I had an experience with a reaction to penicillin in beeswax and peanut oil which indicates the need for a battery of three antigens in order to do allergenic tests in the presence of cutaneous reactions. The man received six daily injections of calcium penicillin in oil and beeswax. A combined urticarial and edematous dermatitis appeared about the tenth day. His reaction was controlled with Benadryl given orally. After the process had cleared up, tests were done both intradermally and epidermally with sodium penicillin (we were unable to obtain calcium penicillin at that time) with peanut oil and beeswax. There was no reaction to the sodium penicillin or to the beeswax. A 30 mm. flare with pseudopods appeared as a reaction to peanut oil. It was believed that in his case he could safely receive penicillin in some other vehicle.

DR. SAMUEL AYRES JR., Los Angeles: My experience with this substance is rather limited; however, I have heard lately that some delayed reactions related to paraffinomas have been observed. I wonder if Dr. Romansky will tell us whether he has observed or heard of any such delayed reactions. Of course, beeswax is not the same as paraffin, not a mineral substance and, therefore, is supposed to be absorbed. I wonder if experimentation on animals has been carried out to the extent of proving how completely the beeswax is absorbed, whether there is any residue and what the likelihood would be of foreign body reactions developing late, say maybe one or two years afterward, because the ease of administration and the other advantages of this type of therapy certainly lend a strong temptation to use this instead of the other method of administration.

DR. MONROE J. ROMANSKY, Washington, D. C.: As regards the incidence of reactions, an important point is whether the mixture is given intramuscularly or subcutaneously. We have given over fifty thousand injections of this material at Walter Reed General Hospital. Patients receive one or two injections a day, depending on what the condition may be. Penicillin in aqueous solution is not used. If the penicillin-oil-beeswax is given subcutaneously there is a greater incidence of local reactions, which, on the basis of the way they respond to treatment, appear to be of an allergic nature. If given intramuscularly, the incidence of allergic reactions is about 3 to 5 per cent. The reactions after subcutaneous administration have at times been treated incorrectly by the use of hot applications, which tend to aggravate. Cold applications or the usual antiallergic therapy, including use of Benadryl, will prevent and minimize these reactions. In patients receiving single daily injections of penicillin-oil-beeswax for about eight days, the allergic reactions tend to occur on the fourth to the twelfth day after the last injection, reaching their peak on the fourth day after initiation and tending to subside thereafter. Penicillin-oil-beeswax has been given for as many as one hundred and fifty consecutive days and been well tolerated by patients. When I first started this work the question of paraffinomas was uppermost in my mind, in view of the history of paraffin when given parenterally. In view of this, biopsy specimens of muscle have been obtained from hamsters, rabbits and human beings who have received the mixture. These biopsy specimens were obtained from one week to six months after the injections. Beeswax tends to disappear somewhere between the tenth and twentieth day by the action of the phagocytes. Paraffin is not removed by phagocytosis. In rabbits, at the end of two to three months only minute oil cysts with thin walls were found. These tended apparently over a period to collapse on the basis of muscle activity. In biopsy specimens taken from 2 patients who expired from other causes about two months after the last injection, all that could be found were two small, 1 to 2 mm., thin-walled oil cysts in 1 patient and a 10 mm. cyst in the other. There was no evidence of beeswax. As far as I know, in the treatment of about 2,000 patients there has been no evidence of a paraffinoma developing. In infants and children, after an injection of the mixture a nodule may be palpable for some time, but I believe that this is usually due to the material being given subcutaneously instead of intramuscularly. To return to Dr. Sulzberger's question on the use of liquid petrolatum, carbowax, aluminum jels and other substances, I originally tried almost all of them. None gave the prolonged blood level that is produced with penicillin-beeswax-peanut oil. It is extremely important that the penicillin blood levels should be those which are therapeutic against the organisms causing the disease which is being treated and that the presence of penicillin in the urine without a satisfactory level in the blood does not suffice.

Special Article

HISTORY OF THE AMERICAN MEDICAL ASSOCIATION

MORRIS FISHBEIN, M.D.
Editor, Journal of the American Medical Association and Hygeia, the Health Magazine
Chicago

(Continued from page 785)

(NOTE.—*Following is the fifth chapter of a history of the American Medical Association, in process of development for publication in connection with the celebration of the Centennial of the American Medical Association in Atlantic City in June 1947.*

The general account of the history of the Association will be followed by individual histories of the various councils, bureaus, publications and other activities of the Association. The general account is written by the editor of THE JOURNAL. *Each of the other historical contributions will be by a member of the individual council, bureau or agency responsible and now associated with it or directly related to its work. Included will be photographs, signatures and a brief biography of each of the hundred presidents of the American Medical Association. This feature has been prepared by Dr. Walter L. Bierring.*

It will be impossible to publish all of the material in THE JOURNAL. *The complete work will be published in book form. It is hoped to have it available by the time of the annual session.*—ED.)

CHAPTER 5. *The First Annual Session*

When President Nathaniel Chapman opened the proceedings of the first annual meeting of the American Medical Association in Baltimore on May 2, 1848 he used strong language in telling the profession of its responsibilities. In these days when organizations throughout the nation are attempting to create popularity for themselves by the practice of what has come to be called "public relations," we hear similar indictments. The words of Dr. Chapman published about a hundred years ago resound almost as if they were of yesterday. He said:

> "This assemblage presents a spectacle of moral grandeur delightful to contemplate. Few of the kind have I ever witnessed more imposing in its aspect, and certainly none inspired by purer motives or having views of a wider range of beneficence. The profession to which we belong, once venerated on account of its antiquity—its various and profound science—its elegant literature—its polite accomplishments—its virtues—has become corrupt and degenerate to the forfeiture of its social position and, with it, of the homage it formerly received spontaneously and universally. . . ."

Dr. Chapman then proceeded to tell the medical profession of his day what has been so frequently told to it in the years that have passed: that the medical profession always cleans its own house, that it does not need extraneous assistance in bringing about reform. Perhaps in anticipation of charges that might be made at some later date, he declined in advance to nomination for reelection to the presidency, saying "Rotation in office, I am persuaded, is the vital principle of every institution in this country. Especially do I consider it so in relation to our own association, national in its objects and constitution. Every section of the country is here represented, and equally engaged in a common cause. No monopoly of honor or privileges must be permitted to any one portion of it. I wish our conduct always to be dictated by liberality, justice and equality."

There were 195 delegates, and the Committee on Nominations was instructed to bring in the names of at least three nominees for each office. Moreover, it was required that the person elected should receive a clear majority of those voting.

The convention turned its attention to the sophistication and adulteration of drugs. Dr. A. H. Stevens of New York was elected President. Then came a number of extraordinary reports of the special committees which had been appointed in previous years. Early in the session Dr. J. C. Warren of Boston, who was first to operate on a patient under ether anesthesia in the Massachusetts General Hospital in 1847, addressed the meeting in reference to the preparation and value of chloric ether as a substitute for sulfuric ether and chloroform, whereupon Dr. F. H. Hamilton of Buffalo introduced a resolution "That, considering the present limited amount of authenticated facts in relation to the danger or safety of anesthetic agents in medicine, surgery and obstetrics, this association is not now prepared to determine upon their value or the propriety of their use, and that the subject be referred to a Special Committee who shall report at the next annual meeting." The resolution was referred to a committee and apparently not made the subject of any later report.

In addition to questions related to medical education and the publication of scientific papers, we find an interesting resolution asking the Committee on Hygiene to direct its attention to the following subjects: First, What is the influence likely to be produced by the extensive introduction of tea and coffee in the diet of persons under the age of puberty? Second, What is the influence of the substitution of the luxuries tea and coffee, as food, on the health of the laboring classes?

The reports of the committees occupy the rest of the volume of the Transactions of the American Medical Association for 1848. Volume I was printed for the Association by T. K. and P. G. Collins in Philadelphia. It contains some documents that are classic.

COMMITTEE ON MEDICAL SCIENCES

The Committee on Medical Sciences, under the chairmanship of W. T. Wragg of South Carolina, reported that it had examined all the journals published during the previous year, that there was too much literature, so that there was an embarrassment in choosing well rather than in collecting abundantly. They did not consider it desirable to limit themselves merely to contributions from America but had collected from all over the world. They then presented some fifty pages of abstracts from the medical literature of the day, dealing with a great variety of subjects.

COMMITTEE ON PRACTICAL MEDICINE

The Committee on Practical Medicine had been charged to report on the more important improvements effected in this country in the management of individual diseases and to report on the progress of epidemics. This committee also had examined the medical periodicals of the day and concluded quite wisely that great discoveries are not really made in any one year. It singled out for special notice a procedure developed by Dr. Gurdon Buck of the New York Hospital which was the multiple scarification of the walls of the throat in the presence of edematous swelling or what was then called "oedematous laryngitis" in its suffocative stage. This, no doubt, was the condition from which George

Washington died and would be called today either "septic sore throat" or "diphtheria."

Then came a rather prolix discussion of epidemics, with special attention to the frightful condition of emigrants coming from Europe, contrasting particularly the nutrition, cleanliness and general hygiene of the German emigrants with that of the Irish, who arrived "in most cases enfeebled from the want of sustenance, and on shipboard, destitute of supplies of wholesome food, depressed of mind, clothed in filthy garments and crowded and confined in air rendered pestiferous by the excrementitious matters eliminated from their own bodies." It called attention to the fact that thousands had perished on the voyages to the United States and Canada. From one ship, the *Virginia,* bound from Liverpool to Quebec, with 470 passengers, 158 were buried at sea.

During the year 1847, 100,000 souls left the British Isles for Canada. More than 5,000 of these died en route and another 8,000 within a few weeks after their arrival. The disease from which these people perished was typhus in its genuine form, and in some ships smallpox, dysentery and measles swelled the amount of mortality. There was much discussion of the ability to distinguish between typhus fever and typhoid fever.

As a supplement to its report the committee included the complete statement of Gurdon Buck on "Oedematous Laryngitis" together with pictures in color of the condition concerned and of the instruments especially designed by him for performing his operation.

THE COMMITTEE ON SURGERY

The Committee on Surgery was supposed to prepare a report on all the important improvements in the management of surgical diseases in America during the year, to which it succinctly replied "Neither brilliant discoveries nor any extraordinary improvements in surgery marked the past year." The committee, nevertheless, decided to make a report of progress, and the major portion of its report deals with cutting for stone and the surgical treatment of aneurysms. Dr. Daniel Brainard of Chicago had found iodine useful as a substance to be injected into infected wounds.

Then comes the report on anesthesia. Eighteen months had elapsed since the introduction of ether by Morton. A large and intelligent body of the medical community, including some of the most eminent surgeons, considered the question settled. They considered the dangers of etherization so inconsiderable as to justify its use prior to all surgical operations. Another class of surgeons wished to limit the use of anesthetics to severe operations and to discourage their general employment. A small portion of the profession objected altogether to the use of anesthetics as dangerous and harmful in their tendency.

The committee refused to take a definite stand. It did, however, offer the opinion of Dr. Henry J. Bigelow of Boston, and it took pride in the fact that anesthesia was an American contribution. At the same time the committee noted with regret that the early history of the discovery "is encumbered with angry disputes amongst rival claimants for the honor, and that attempts were made by those most intimately interested in the claim. . . ." Much consideration is given to the claims of Horace Wells, but it is stated clearly that Wells abandoned his experiments begun in 1844, and that the first successful experiment was performed by William T. G. Morton, a dentist of Boston, on a patient from whom he extracted a tooth on Sept. 30, 1846. Dr. Henry J. Bigelow had read a paper in Boston on Nov. 3, 1846. It was published in the *Boston Medical and Surgical Journal* November 18. Within six weeks of the publication of that paper, ether had been tested and was being warmly advocated among surgeons in London. The report then lists all the various surgeons in the United States who had already used ether in surgical operations and it was noted that fatal effects following the use of chloroform had been more frequent than from ether.

Incidentally the committee reported also that it had received a number of letters about the curability of cancer and the results of operations on this class of tumors, but apparently this was too much for the committee and it made no report but merely submitted the letters to the convention.

COMMITTEE ON OBSTETRICS

The Committee on Obstetrics had the duty of preparing a report on all the important improvements in obstetric art and of the management of diseases peculiar to women and children. Obviously the matter of chief concern was the use of the anesthetics in childbirth. The committee got itself into the usual argument that labor is a physiologic or natural process and that pain should therefore be endured, but the committee attached little importance to this objection. It wisely decided that if one adopted that point of view it would be impossible even to give remedies to the parturient woman. Already anesthetic agents had been used in 2,000 cases and, as far as the committee was able to learn, without a single fatal result and few, if any, untoward results.

The committee also suggested that doctors try out chloroform on themselves as a means of dispelling their vague apprehensions in relationship to it. Indeed the committee recommended that the doctor begin with 20 to 30 drops and gradually increase the quantity to find out how to use the chloroform safely and to acquire tact and confidence in giving it to others.

There was much discussion of the relative advantages of ether and chloroform for different types of cases, chloroform being considered more convenient and ether safer, but both efficient.

To this report were appended half a dozen communications from practitioners who had used anesthetics in labor.

COMMITTEE ON MEDICAL EDUCATION

The Committee on Medical Education was charged with preparing a report on the general condition of medical education in the United States in comparison with medical education in other enlightened nations and to note particularly the quality of instruction, the number of pupils and the requirements in various states.

The committee pointed out that in most foreign countries the standard of qualifications necessary for a doctorate in medicine was higher than in the United States and that the preliminary education was broader and more thorough. As a result of the previous meeting of the American Medical Association, some medical schools had already lengthened their curriculums and added other courses of instruction. Incidentally, the committee noted that in Harvard University candidates who had not received a college education were subjected to an examination on natural philosophy and the Latin language and were required to translate *ad aperturam libri* Cicero's orations. The same practice was followed in the medical societies of Massachusetts in their examinations for licenses to practice.

The committee had already decided that there were too many doctors in the United States, the proportion being five times as great as in France. It was urged that private teachers exercise greater circumspection of students taken into their offices. The committee felt that the oversupply of doctors was largely responsible for the rise of quackery and charlatanism, and it urged that a proper medical education could be had only by spending a certain amount of time in a hospital in the actual care of patients.

COMMITTEE ON MEDICAL LITERATURE

Looking back on the perspective of one hundred years, the report of the Committee on Medical Literature, under the chairmanship of Oliver Wendell Holmes and including such distinguished men as Enoch Hale, G. C. Shattuck Jr., Daniel Drake, John Bell, Austin Flint and W. Selden, merits first place. There are some sections so clearly of the style and manner of thought of Oliver Wendell Holmes that they merit frequent quotation. There is an adequate record of the history of medical publications in the United States, with complete reports of existing medical journals.

A typical medical journal of the time is thus described:

> The first part of each number is devoted to original articles, consisting of essays, histories of epidemics and endemics, series of cases and single cases, and accounts of operations. Occasionally a more detailed and comprehensive history of some disease is introduced under the name of *monograph*, and not unfrequently extensive statistical tables are given, bearing especially upon surgical and obstetrical practice. Then follow *Reviews* or formal examinations of works recently published, usually analytical in character and having for their principal object the book rather than the general subject of which it treats. To this division succeeds a miscellaneous and heterogeneous assemblage of *bibliographical notices;* the sweepings of the critical *atelier;* the rinsings and heeltaps of the critical banquet; a necessary part of the editor's prospectus, but one which is least gratifying to minute inspection. Here the importunate friend receives his expected compliment, the dull dignitary is pacified with his scanty morsel of eulogy, the Maecenas is paid in fair words for his patronage; the book which must be noticed and has not been read is embalmed in safe epithets and inurned in accommodating generalities. Lastly, a considerable part of the number is made up of selections, either taken promiscuously from other journals and recently published works, or, in the better managed periodicals, classified so as to present a summary of the recent progress of science in its several departments.

The committee found that a great proportion of a medical journal was made up of quotations from other medical journals, so that all the medical journals were a good deal alike, since there were very few original articles published of any merit and they were found again and again repeated in the medical journals.

Following the discussions of the periodicals come discussions of the books in each of the important medical subjects and then in some half dozen pages a witty analysis of medical writings, classic in its diction and in its consideration. Special attention was paid to the so-called introductory lectures, which are really the opening statements delivered by the deans or professors in the medical schools to the incoming students. Says the report:

> They must not be judged too harshly, for they are delivered to young men, who like high seasoning, and they naturally partake somewhat of the character of advertisements. Many of them are agreeable and appropriate performances, but others are open to severe comment. Turgid and extravagant attempts at eloquence, a fondness for effete Latin quotations, a parade of scholastic terms where simple ones only are called for, an inclination to adopt the cant phrases of political and literary writers, are the common faults of these productions. The physician should remember, that his style has no more occasion for pomp of oratory and glitter of epithet, than his costume for the gold lace and feathers which belong to the military chieftain. Nothing is more offensive than an attempt to tell that which should be said plainly and decently, in high flown language. It vitiates the taste of the student who listens to it or reads it, and exposes the profession to derision from those who cannot value the important truths disguised by such ill chosen finery.

COMMITTEE ON PUBLICATION

The Committee on Publication, headed by Isaac Hays, reported that it had printed 2,500 copies of the Conventions of 1846 and 1847 and they still had 800 copies left.

There is a complete list of the members who paid $3 each for membership in the Association. Then come a number of communications dealing with the ethics of the pharmaceutical profession and an exposé of the adulteration and falsification of drugs sold in the United States.

The committee, which had been supposed to ascertain the total number of doctors in the United States, reported for the states of Virginia, Delaware and Massachusetts. And finally there were two scientific papers and lists of the officers and members of the American Medical Association.

A good index completed what is even for these times an extraordinarily interesting volume.

(To be continued)

Clinical Notes, Suggestions and New Instruments

HAY FEVER AND ASTHMA FOLLOWING MAXIMUM EXPOSURE TO RAGWEED

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Newark, N. J.

According to Durham,[1] the highest ragweed pollen count in the United States has been recorded near Indianapolis. Clinical corroboration of this observation was afforded me when I was stationed for the ragweed seasons of 1944 and 1945 at Wakeman General Hospital, Camp Atterbury, Ind., some 35 miles south of Indianapolis.

The following case report is illustrative of many of a similar nature which will plague the Disability Rating Boards of the Veterans Administration for many years, requiring solomonic wisdom for fair adjudication both for the veteran and the government.

REPORT OF CASE

A white soldier aged 21 was admitted on Aug. 26, 1944 to the allergy ward of Wakeman General Hospital, Camp Atterbury, Ind. He had been affected by severe sneezing, stuffed nose, redness and watering of the eyes for the past week. There was no previous history, personal or familial, of hay fever, asthma or other allergic manifestations. However, the patient admitted he could have had mild sneezing in the summer or autumn without distinctly recollecting it. This was his first summer in the middle west; previously he had always resided in Newark, N. J.

Physical examination on admission revealed that the patient had severe symptoms of hay fever with a pale, boggy, intensely swollen nasal mucosa, injected conjunctivas and a right otitis media, nonsuppurative. Intracutaneous ragweed tests were decidedly positive. Serologic tests and urinalysis were normal. The blood count was normal except for a 10 per cent eosinophilia.

1. Durham, O. C.: The Pollen Count of the Air in North America, J. Allergy **6**: 128 (March) 1935.

Acute symptoms of hay fever persisted for about two weeks, than subsided gradually. No relief was afforded by ephedrine nose drops or ephedrine-phenobarbital capsules. The patient was reclassified for limited service, than returned to duty on Sept. 27, 1944.

He did well until Oct. 23, 1944, when he was readmitted to the allergy ward. This was well past the end of the ragweed season for that area. He had been wheezing for the past few hours. Nasal and ocular symptoms were absent, and this was the first asthma attack he had ever experienced.

Physical examination revealed a patient with moderate asthma; the lungs showed asthmatic rales and breath sounds throughout. The ear, nose and throat consultant reported that the nose showed swelling of the turbinates, especially the right, bathed in watery secretions. Purulent secretion or polyps were not observed. The frontal sinuses transilluminated clear, the antrums fair.

Laboratory procedure disclosed the following: A roentgenogram of the chest revealed normal conditions. A roentgenogram of the sinuses revealed a circumscribed, rounded density arising from the floor of the right maxillary antrum, and another from the medial wall, representing a polyp formation or mucocele. Only a small amount of aeration was visualized in the upper portion of the antrum. There was thickening of the lining membrane of the ethmoidal cells on the right side. The remainder of the paranasal sinuses showed normal aeration throughout. Urinalysis and serologic tests were normal. The blood count was normal except for an 11 per cent eosinophilia. Thirty-six intracutaneous dermal tests with common inhalants, contactants, epidermals and foods were negative except for buckwheat, which was decidedly positive; orange, moderately positive, and ragweed, slightly positive. (Ragweed was definitely positive during the ragweed season.)

The patient was placed on a diet without buckwheat and citrus fruits, and ephedrine sulfate-phenobarbital capsules and saturated solution of potassium iodide were administered three times a day. Moderately severe asthma which required epinephrine injections at least once a day persisted for about ten days. The attacks tapered off, averaging about one a week for the next six weeks. A repetition of the blood smear at this time disclosed an eosinophilia of 8 per cent. Examination of the nose revealed slightly pale and boggy nasal mucosa, though nasal and paranasal symptoms had not been observed for the past two months. A follow-up roentgenogram of the sinuses showed moderate clouding toward the floor of the right antrum caused by membranous infiltration or congestion; the sinuses were otherwise normal. On Jan. 8, 1945, after a three week symptom-free period, the patient was given a medical discharge from the Army because of bronchial asthma.

The patient was next seen, after he and I had both become civilians, in my office in Newark, N. J., on May 13, 1946 (sixteen months later). He had been perfectly well until one month previous, when he had begun to observe difficulty in breathing at night. There had not been any nasal or paranasal symptoms or other manifestations of allergy. He had been on a normal diet.

Examination revealed a well developed man who appeared to be breathing normally. The lungs showed a slight prolongation of the expiratory phase of respiration throughout, with no rales. The nasal mucosa was slightly pale and boggy. Intracutaneous allergy tests gave slight positive reactions to dust, mixed trees, timothy and ragweed.

COMMENT

In all probability this patient will now require prolonged allergic management. The problem arises as to whether he and others like him are entitled to medical care from the Veterans Administration and to disability ratings if the asthma is of sufficient frequency and intensity. The Veterans Administration, in many cases, reasons that the person is potentially allergic because of hereditary factors. The allergic chain of symptoms could certainly have developed whether or not the patient was in the armed forces. On the other hand, the ragweed-sensitive patient who is stationed in an area of dense ragweed pollination may suffer accentuation of various allergic symptoms for many years. The patient states, and in my opinion justly, that if he was not in the Army he would never have moved to such an area. The problem is extremely complex, and there are as many different decisions as there are Veterans Rating Boards. To insure fairness to all concerned, decisions in cases of this type should be made by trained allergists.

SUMMARY

A case of hay fever followed by asthma occurred after maximum exposure to ragweed pollen in a soldier who had previously lived in an area with a much lower ragweed pollen content. Previously he had not had hay fever or other allergic clinical symptoms. The problem of medical care and compensation for veterans in cases of this type is one which will face the Disability Rating Boards of the Veterans Administration for many years.

33 Johnson Avenue.

Council on Foods and Nutrition

The question of the essentiality of fatty acids in human nutrition is discussed in this article. It was prepared by the authors at the request of the Council and has been authorized for publication.

JAMES R. WILSON, M.D., *Secretary.*

ESSENTIAL FATTY ACIDS AND HUMAN NUTRITION

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Interest with regard to the significance of fat in the diet was evidenced even by early investigators in the field of nutrition, and these workers were led to believe that the only role of dietary fat was to serve as a rich source of calories. Later observers, however, emphasized its additional importance as a source and as a vehicle for the absorption of certain vitamins. In 1929 the Burrs [1] discovered the essential nature of certain fatty acids in the nutrition of the rat. For the first time, then, a specific function could be attributed to fat other than its energy producing property and its action as a vitamin carrier. It must be emphasized that the observation proving linoleic acid and arachidonic acid to be dietary essentials was not made until young laboratory animals had been maintained on diets extremely low in fat for relatively long periods of time. The likelihood that a human infant would subsist for a prolonged period on a diet practically devoid of fat, yet complete as regards other known dietary essentials, is practically nil. Hence the recognition in infants and children of any characteristic clinical picture or type of malnutrition which may result from the specific lack of certain fatty acids in the diet has not been demonstrated conclusively.

In this presentation, in addition to a consideration of the experimental results which have been observed with laboratory animals on low fat diets, as well as the effect of the administration of certain fatty acids to these animals, an attempt will be made to summarize the data which have a bearing on the possible importance of the essential fatty acids in human nutrition.

From the Department of Pediatrics, University of Texas School of Medicine (Dr. Hansen), and the Division of Physiological Chemistry, University of Minnesota School of Medicine (Dr. Burr).

1. Burr, G. O., and Burr, M. M.: A New Deficiency Disease Produced by the Rigid Exclusion of Fat from the Diet, J. Biol. Chem. **82**: 345, 1929; On the Nature and Role of the Fatty Acids Essential in Nutrition, ibid. **86**: 587, 1930. Burr, G. O.; Burr, M. M., and Miller, E. S.: On the Fatty Acids Essential in Nutrition, ibid. **97**: 1, 1932.

It is quite evident that the method of approach for establishing the human need for these fatty acids cannot be the same as that used for experimental animals. Furthermore, the fact that adequate direct methods for determining the amount of linoleic and arachidonic acids in blood serum and animal tissue have not been available has been an additional handicap in the prosecution of studies with human subjects. Consequently, much of the evidence we have for the human need for the essential fatty acids is indirect.

ESSENTIAL NATURE OF FATTY ACIDS IN ANIMAL NUTRITION

The term "essential fatty acid" was introduced in 1930 and since that time has been used to designate a group of unsaturated fatty acids which will stimulate renewed growth of rats after they have reached a plateau on a low fat diet. Careful exclusion of the essential fatty acids from the diet in rats leads to (1) development of scaly skin and caudal necrosis, (2) decided retardation of growth, (3) increased water consumption and (4) early death. Any or all of these signs may be used for a quantitative assay of the needs for essential fatty acids. Other more or less specific effects of the deficiency are histologic changes in the ovaries, uterus and other tissues; poor ovulation, reproduction and lactation in the female, male sterility, high respiratory quotients and high metabolic rates, kidney lesions and hematuria. The scaly skin in rats, which is very striking in a dry climate, may be suppressed by high humidity. The time of appearance of the first definite symptom (scaly skin) depends largely on the amount of unsaturated acids stored in the body fat of the young. Hence any animal which has had access to a high fat diet before the experiment is started will maintain its normal appearance for a long time because of the low rate of metabolic use of stored essential fatty acids.

TABLE 1.—*Purified Fatty Acids Tested for Activity in Curing Fat Deficiency in Small Animals*

Positive Response	Negative Response
Linoleic	All saturated acids
Linoleyl alcohol	Oleic
Linolenic	Elaidic
Arachidonic	12-Oleic
Docosahexenoic *	Erucic (13-docosenoic)
Hexahydroxystearic	Ricinoleic (12-hydroxyoleic)
	Linolelaidic
	9,11-Linoleic
	α Eleostearic (9,11,13-linolenic)
	Dioxidostearic
	Trihydroxystearic
	Tetrahydroxystearic
	Chaulmoogric
	Clupanodonic † (Octa decatetrenoic)

* Not purified by crystallization but by fractional distillation of the ester.
† This preparation was found to be toxic.

In table 1 are listed [2] the purified fatty acids that have been tested for their activity in curing a fat deficiency in small animals. Some of these acids have been used only once in a few animals. Linoleic, linolenic and arachidonic acid have been studied most extensively. Linolenic acid and the higher acids of fish oil bring about renewed growth in rats without curing the skin. Only linoleic acid and arachidonic acid give complete cures, but, strictly speaking, only one of these is essential. If either linoleic or arachidonic acid is added to the diet, a complete cure of the deficiency symptoms will take place. However, since linoleic acid is of plant origin and arachidonic is of animal origin, the former should be considered the primary dietary essential.

The rate of use of these unsaturated fatty acids determines the level of requirement. It has been found that prophylactic daily doses of about 20 to 25 mg. of linoleic acid promote good growth and reproduction in rats, but for optimum lactation 100 mg. is recommended. In curative experiments 50 to 100 mg. daily appears to be distinctly superior to lower doses. Assuming that the minimum adequate daily intake of linoleic acid is 100 mg. for a rat consuming 10 Gm. of diet, the linoleic acid requirement can be set at about 1 per cent of the diet. Since it has not yet been possible to establish the requirement for man through direct experimentation, a corresponding level of intake (1 per cent of the diet) has been recommended in human nutrition on the assumption that human beings and rats have the same metabolic requirement for this food factor.

By far, most of the work on the essential fatty acids has been done on the rat as an experimental animal. However, Hansen and Wiese [3] found in maintaining young dogs on a low fat diet that the most striking observation with these animals was the development of dryness of the hair and skin and flaky desquamation of the skin. Addition of fresh lard to the diet resulted both in preventing the appearance of these conditions and in restoring the abnormal skin to a normal state. A fat deficiency syndrome characterized by disturbance in growth, a dandruff-like dermatitis and early death also has been produced in mice.[4] These symptoms were cured by the addition of lard to the diet.

STUDIES BEARING ON RELATION OF UNSATURATED FATTY ACIDS IN HUMAN SUBJECTS

Experimental Use of Diets Very Low in Fat.—Clinical Observations: Comparatively few studies with human subjects have been carried out in which the effect of diets extremely low in fat has been observed for an extended period of time. Von Gröer [5] in 1919, prompted by Aron's study with rats on low fat diets, maintained 2 infants on a diet of skim milk for a period of nine months. He observed that both infants showed poor growth but attributed this to a respiratory tract infection from which both infants suffered severely and for a much longer time than other infants who were similarly affected in the hospital ward. One of the children on the low fat diet developed evidence of exudative diathesis, and the diet was discontinued because of the lack of appetite. Holt and his co-workers [6] in 1935 kept 3 infants aged 4 to 6½ months on a diet containing about 1 Gm. of fat per day for two to seven days. One of these infants, they noted, developed spasmodic bronchitis and an eczematous eruption, which cleared when fat was restored to the diet and recurred when fat was again eliminated. Apparently the authors did not consider this phenomenon a mere coincidence. In 1937 Chwalibogowski [7] reported having maintained 2 infants from birth to

2. Burr, G. O.: Significance of the Essential Fatty Acids, Fed. Proc. **1**: 224, 1942.

3. Hansen, A. E., and Wiese, H. F.: Studies with Dogs Maintained on Diets Low in Fat, Proc. Soc. Exper. Biol. & Med. **52**: 205, 1943.

4. White, E. A.; Foy, J. R., and Cerecedo, L. R.: Essential Fatty Acid Deficiency in the Mouse, Proc. Soc. Exper. Biol. & Med. **54**: 301, 1943.

5. von Gröer, F.: Zur Frage der praktischen Bedeutung des Nährwertbegriffes nebst einigen Bemerkungen über das Fett minimum des menschlichen Säuglings, Biochem. Ztschr. **93**: 311, 1919.

6. Holt, L. E., Jr.; Tidwell, H. C.; Kirk, C. M.; Cross, D. M., and Neale, S.: Studies in Fat Metabolism: Fat Absorption in Normal Infants, J. Pediat. **6**: 427, 1935.

7. von Chwalibogowski, A.: Experimentaluntersuchungen über kalorisch ausreichende, qualitativ einseitige Ernährung des Säuglings, Acta pædiat. **22**: 110, 1937.

13 and 15 months of age on a diet consisting of skim milk, sugar and cereal. Later, fruit compote and carrots were added to the diet, and both children were given ultraviolet radiation at various intervals. Although no skin manifestations are described by the author for either child, both were found to be anemic when 11 to 12 months old and both suffered from repeated infections. During the fifteen months observation, 1 child had two attacks of grip, 2 of sore throat and 1 of pyuria. The other child had sore throat, grip and measles. The low fat diet in the latter instance was discontinued at the end of thirteen months because of lack of appetite. During none of these observations were any attempts made to determine the kind or amount of fat synthesized by the body.

Hansen and his co-workers have had the opportunity to observe the effect of a practically fat free diet on 4 human subjects. Preliminary observations were made with 2 normal infants for a period of ten weeks. Both infants suffered from attacks of impetigo and prickly heat which were resistant to the usual forms of treatment. Brown, Hansen, Burr and McQuarrie [8] in 1938 reported studies on an adult subject who was observed for a period of six months while on a low fat diet. When this same diet was fed to young rats, they developed the typical fat deficiency syndrome. Subjectively, in the adult under observation the most striking effect was the absence of the sensation of fatigue and a decrease in the migraine-like headaches from which he had suffered periodically. The respiratory quotient showed a slight increase, which response was similar to that noted in rats. The fourth instance [9] in which an extremely low fat diet was used for a prolonged period in a young human subject was that of a child with chylous ascites. The diagnosis was made when the child was about 3 weeks of age, at which time about a liter of creamy fluid was removed from the peritoneal cavity. Because the absorbed fat could not enter the blood stream, it was believed that placing the child on a low fat diet might decrease the fluid accumulation in the abdominal cavity. At first the diet consisted of concentrated skim milk and the usual vitamin supplements, but later vegetables and cereals were added. He was maintained on this type of regimen until he was 23 months of age. Although growth and development of the patient were fairly satisfactory, he never had the appearance of a robust child. He acquired a number of respiratory infections, and it appeared to the staff physicians that he reacted to these more severely than is normally expected. The most striking clinical finding, however, was with reference to the skin. The child became afflicted with impetigo on two occasions, and these infections were much more difficult to clear up than those encountered in the other infants in the same ward who were similarly affected. During his first summer, at the age of about 8 months, he developed a prickly heat eruption, which dermatitis persisted for months into the cooler weather, long after other infants in the same ward having the same type of rash had recovered. During the last half of the first year he developed eczematous patches on his body and face at various times, but these responded quite well to treatment with crude coal tar ointment.

In summary, on the basis of the work of various authors regarding clinical observations with human subjects maintained on diets very low in fat, it is apparent that no specific clinical syndrome develops during a period of one to two years. It may be pointed out, however, that the duration of sustenance on this type of diet in the patients studied thus far is short compared with the length of time that is necessary to produce distinct symptoms in experimental animals. Even in the diet of the experimental animal evidence of lack of fat in the diet requires a relatively long time to develop. For example, in the rat symptoms and signs do not develop until about one-half of the time from birth to maturity. Likewise in the dog the interval for the development of dermatologic signs is almost as long, relatively. Human infants maintained on low fat diets even for the periods mentioned are only one-sixth to one-eighth of the period from birth to maturity, or, comparatively speaking, one-third of the time required to develop a deficiency in experimental animals.

Serum Lipid Studies in Patients on a Low Fat Diet: Early observations of Hansen and Burr [10] showed that the serum lipids of rats suffering from the fat deficiency syndrome had lower iodine numbers than those of control animals. Likewise, in the preliminary studies of Hansen with the 2 infants on a low fat diet a similar decrease from the normal was noted in the iodine value of the blood fat. Periodic determination of the serum lipids in the patient with chylous ascites revealed the iodine values of the total fatty acids to be definitely lower than those of normal infants. The degree of unsaturation of the fat in both the acetone insoluble (phospholipid) and acetone soluble (glyceride + cholesterol ester) fractions was abnormally low. On one occasion it was possible to separate the triglyceride fatty acids from the cholesterol ester fatty acids, and in this instance it was found that the iodine numbers of the fatty acids in both portions were low. Studies by Wiese and Hansen [11] with dogs on low fat diets revealed that the greatest drop in the iodine number appears in the cholesterol ester fatty acids. Normally the cholesterol ester fatty acids are the most highly unsaturated of the fatty acids in the blood serum. The iodine number of the total fatty acids in the adult subject was also found to be decreased while on the low fat diet. It was possible to brominate the fatty acids in the serum in this case, and the findings with regard to the linoleic and arachidonic acids expressed as percentages of the total fatty acids are given in table 2.

TABLE 2.—*Linoleic and Arachidonic Acids Expressed as Percentages of Total Fatty Acids*

	Arachidonic Acid	Linoleic Acid
Normal diet	3.2	5.7
Low fat diet (for six months)	1.87	3.2

In all the serum lipid studies of the subjects on low fat diets it was found that the total amount of fatty acids in the various fractions has been within normal limits. It appears from these data that the animal organism is able to synthesize sufficient fat to maintain a normal level of blood lipid but apparently is unable to synthesize certain highly unsaturated fatty acids.

Relatively Low Fat Intake Because of Faulty Absorption.—Well controlled experiments which attempt to determine the effect of the lack of dietary fat on human

8. Brown, W. R.; Hansen, A. E.; Burr, G. O., and McQuarrie, I.: Effects of Prolonged Use of Extremely Low Fat Diet on an Adult Human Subject, J. Nutrition **16**: 511, 1938.

9. Hansen, A. E., and Wiese, H. F.: Clinical and Blood Lipid Studies in a Child with Chylous Ascites, Am. J. Dis. Child. **68**: 350 (Nov.) 1944.

10. Hansen, A. E., and Burr, G. O.: Iodine Numbers of Serum Lipids in Rats Fed on Fat Free Diets, Proc. Soc. Exper. Biol. & Med. **30**: 1201, 1933.

11. Wiese, H. F., and Hansen, A. E.: Distribution of Fatty Acids in the Blood Serum of Dogs as Affected by Diet, Fed. Proc. **3**: 97, 1944.

subjects are relatively meager; however, there are important clinical conditions in which a defect in fat absorption is present. In patients with steatorrhea not only is there faulty absorption of fat, but, in addition, these patients often are advised to use low fat diets and there results a situation which is equivalent to maintenance on a diet quite low in fat. This condition usually exists for a prolonged period. It has long been known that patients having difficulty with absorption of fat may develop a deficiency state of one type or another. However, it has never been fully ascertained whether or not the malnutrition which is seen in patients with idiopathic steatorrhea or the celiac syndrome may be due in part to the specific lack of certain fatty acids. A clinical observation which is often made in some cases of a prolonged steatorrhea is the presence of dermatologic abnormalities. This observation may be of some importance in view of the fact that in experimental animals one of the chief manifestations of a fat deficiency is the development of an abnormality of the skin. In 1932 Bennett, Hunter and Vaughan [12] reported the presence of skin eruptions in 7 cases of idiopathic steatorrhea. These authors state that "The frequent occurrence of skin lesions appears too striking to be mere coincidence." Konstam and Gordon [13] also confirm this observation and report pruriginous vesicular dermatitis in a man aged 55 with steatorrhea. Riley [14] reports the finding of "large circumscribed erythematous areas" in a boy aged 17 years with idiopathic steatorrhea. In a 1944 report by Luzzatti and Hansen [15] on 10 infants and children in whom the diagnosis of celiac syndrome was made, 3 of the patients showed evidence of macular rash or eczematous lesions. Further evidence that some of the above patients possibly may actually suffer from the lack of specific fat is suggested by blood lipid studies. The authors found that the iodine number of the fatty acids in patients with the celiac syndrome was exceptionally low, 70 to 86, compared with the normal range of 98 to 113 for their control subjects in the same age group. The amount of fatty acid in the various fractions of the blood lipids was essentially normal, but the degree of unsaturation was abnormally low in all fractions. This indicates again that these patients can synthesize saturated fatty acids from sources other than dietary fat but are unable to synthesize unsaturated fatty acids to a sufficient extent to maintain the normal degree of unsaturation of the blood lipids. The establishment of a normal range for the iodine number of the serum fatty acids in human subjects and the possible nutritional significance of maintaining this degree of unsaturation in the blood is further suggested by the clinical findings and blood lipid analyses in patients with eczema.

Study of Patients with Eczema.[15a]—It was first reported in 1933 by Hansen [16] that some infants with eczema appeared to be definitely benefited clinically when fats containing the essential fatty acids were added to the diet. This observation led to a study of the blood lipids of eczematous and normal noneczematous infants and children. It has been found by Hansen and his co-workers and also by Finnerud, Kesler and Wiese [17] using some 150 noneczematous control subjects and 180 eczematous patients that while there is no significant difference in the total amount of fat in the serums of the two groups of individuals the relative degree of unsaturation of the serum fatty acids in the patients with eczema is definitely less than in that of control subjects. The serum fatty acids of 82 per cent of infants under 2 years, 74 per cent of children from 2 to 15 years and 55 per cent of older subjects show iodine numbers below the normal range of 95 to 130. These findings have been confirmed by Faber and Roberts [18] as well as by Schornstein.[19] On the other hand, Ginsberg, Bernstein and Iob [20] found no difference between the iodine number of the serum fatty acids for patients with infantile eczema and those for normal subjects.

Pooled samples of lipid extracts of the serum were studied by Brown and Hansen [21] wherein it was found that the content of arachidonic and linoleic acid was less in the patients with eczema than in the pooled samples of the lipid extract of control subjects. These acids were determined as polybromides and tetrabromides and the values as percentage of the total fatty acids in the serums are summarized in table 3.

It has been found further by Hansen,[16] by Cornbleet and Pace,[22] by Finnerud, Kesler and Wiese [17] and by Ginsberg, Bernstein and Iob [20] that the addition of fats rich in linoleic and arachidonic acid such as fresh lard, corn oil and raw linseed oil to the diet of eczematous patients has resulted in a definite amelioration of the skin eruption in a considerable portion of the patients and in a complete clearing of the skin in some instances. In most of the patients studied by Hansen and by Finnerud and his co-workers the skin eruptions were resistant to the usual forms of therapy, yet more than 50 per cent of these patients have shown great improvement. The clinical response to the addition of one of these fats to the diet has been most evident in those cases in which the iodine number of the blood fat has been below the normal range. Improvement in the condition of the skin has usually been accompanied by a rise in the iodine number of the serum fatty acids to a normal level. Whether or not these responses in the condition of the skin of eczematous patients to the ingestion of fat containing the essential fatty acids accompanied by a rise in the iodine number of the serum fatty acids is a result of supplying

TABLE 3.—*Arachidonic and Linoleic Acid in Patients with Eczema*

Pooled Samples	Arachidonic Acid % of T. F. A.	Linoleic Acid % of T. F. A.
35 control subjects	2.83	4.80
12 control subjects	2.90	5.20
18 young patients with eczema	1.34	3.20
8 adult patients with eczema	1.60	4.20

12. Bennett, T. I.; Hunter, D., and Vaughan, J. M.: Idiopathic Steatorrhea (Gee's Disease): A Nutritional Disturbance Associated with Tetany, Osteomalacia and Anemia, Quart. J. Med. **1**: 603, 1932.
13. Konstam, G., and Gordon, H.: Idiopathic Steatorrhea with Skin Lesions and Megalocytic Anemia, Proc. Roy. Soc. Med. **29**: 629, 1936.
14. Riley, I. D.: Metabolic Eczema in Idiopathic Steatorrhea, Lancet **1**: 262, 1939.
15. Luzzatti, L., and Hansen, A. E.: Study of the Serum Lipids in the Celiac Syndrome, J. Pediat. **24**: 417, 1944.
15 a. The expression "eczema" is used advisedly, and this phase of the subject is discussed in greater detail in a paper to appear in the American Journal of Diseases of Children.
16. Hansen, A. E.: Serum Lipid Changes and Therapeutic Effects of Various Oils in Infantile Eczema, Proc. Soc. Exper. Biol. & Med. **31**: 160, 1933; Serum Lipids in Eczema and in Other Pathologic Conditions, Am. J. Dis. Child. **53**: 933 (April) 1937; Evaluation of the Nutritional Status of Children, with a Note on the Unsaturated Fatty Acids in Nutrition, J. Omaha Mid-West Clin. Soc. **4**: 48, 1943.
17. Finnerud, C. W.; Kesler, R. L., and Wiese, Hilda F.: Ingestion of Lard in the Treatment of Eczema and Allied Dermatoses, Arch. Dermat. & Syph. **44**: 849 (Nov.) 1941.
18. Faber, H. K., and Roberts, D. B.: Studies in Infantile Allergic Eczema: Serum Lipids, with Special Reference to Saturation of the Fatty Acids, J. Pediat. **6**: 490, 1935.
19. Schornstein, L.: Ueber den Gehalt der Serumfette an ungesättigten Fettsäuren beim Säuglingsekzem, Ztschr. f. Kinderh. **59**: 52, 1937.
20. Ginsberg, J. E.; Bernstein, Clarence, Jr., and Iob, L. Vivian: Effect of Oils Containing Unsaturated Fatty Acids on Patients with Dermatitis, Arch. Dermat. & Syph. **36**: 1033 (Nov.) 1937.
21. Brown, W. R., and Hansen, A. E.: Arachidonic and Linoleic Acid of the Serum in Normal and Eczematous Human Subjects, Proc. Soc. Exper. Biol. & Med. **36**: 113, 1937.
22. Cornbleet, T., and Pace, E. R.: Use of Maize Oil (Unsaturated Fatty Acids) in the Treatment of Eczema, Arch. Dermat. & Syph. **31**: 224 (Feb.) 1935.

a deficiency of these fatty acids is not definitely established, but the evidence seems to indicate that there may be either a very low intake or an abnormally high requirement of these patients for unsaturated fatty acids which are not synthesized by the body. Epstein and Glick [23] and also Taub and Zakon [24] found no beneficial effects which could be attributed to the ingestion of linseed oil.

It has been observed by a number of clinicians that infantile eczema is less prevalent in breast fed infants than in partially breast fed or artificially fed infants. Grulee and Sanford [25] in a five year study of 20,061 babies found eczema to occur seven times more frequently in artificially fed than in breast fed infants. Robinson [26] also noted skin rashes to be less common in breast fed infants than in infants receiving various formulas containing evaporated milk. In this connection it is interesting to note that Hilditch and Meara [27] in 1944 reported higher percentages of linoleic and unsaturated C_{20-22} acids in human milk fat than in cow's milk fat. Preliminary studies undertaken in 1935 by W. R. Brown and the authors to determine the arachidonic and linoleic acid content of breast milk of mothers nursing eczematous infants showed that the values for these fatty acids tended to be somewhat lower than those for the breast milk of mothers nursing infants with no skin eruption.

COMMENT

In regard to clinical observations made thus far with human subjects, there is no evidence to indicate that a lack of the essential fatty acids produces a disturbance in growth, hematuria, kidney lesions, impaired reproduction, lactation or sterility, which abnormalities are attributed to the dietary lack of either linoleic or arachidonic acid in small experimental animals. However, as one of the most characteristic findings in all animal studies is an alteration in the appearance and character of the skin, it is perhaps not surprising to find a possible relationship between dietary fat and the skin in some human subjects.

The evidence from studies with human subjects on low fat diets for periods up to two years is not very striking in regard to the possible development of an abnormality of the skin. However, the child with chylous ascites who was maintained for the longest time on a low fat diet did develop some eczematous-like lesions and did have more difficulty than expected with both impetigo and prickly heat. This would be in line with observations of Hansen and Wiese [28] with dogs wherein it was found that the skin of animals on a fat free diet appeared to be less resistant to impetiginous infections than animals receiving fresh lard in the diet. That the unsaturated fatty acids may be concerned with the natural integrity of the skin in the healthy state is suggested further by the observation of patients with chronic eczema. The true therapeutic significance, limitations and indications for the addition of substances such as fresh lard or vegetable oils to the diet of these subjects has not been completely evaluated. However, the overall experience of Hansen with approximately 120 patients, all of whom were suffering from an intractable form of eczema and all of whom received supplements of a fat or oil rich in the essential fatty acids, indicates that this type of therapy may be a useful adjunct in this condition. Of the patients who have been studied long enough to interpret the results, in about one half the improvement in the condition of the skin has been excellent, in one fourth the improvement has been definite and in the remaining fourth there has been little or no change observed. No relationship between unsaturated fatty acids and allergy has been demonstrated.

Although the specific function of the essential fatty acids in maintaining a healthy skin, if such a function exists, is not known, their importance in this respect is further evidenced by the work of Hansen, Wiese, Kooda and Fredericks [29] with dogs. These authors found that the skin of young dogs receiving fresh lard in the diet was definitely more resistant to the effect of the local application of croton oil in acetone than the skin of animals which received the same diet except for the isocaloric substitution of sucrose for the lard.

The nature of the histopathologic changes which have been shown to result from the lack of unsaturated fatty acids in the diet of animals is such that it is very unlikely that these will prove to be of any value in the recognition of a fatty acid deficiency in human subjects. The metabolic response as evidenced by the respiratory quotient in an adult subject on the fat free diet was similar to that observed in rats on a fat free diet. Nothing is known regarding interrelationships between the unsaturated fatty acids and the various vitamins in human subjects, although an extensive literature is accumulating from animal experiments. For example, the specific good effect of linoleic acid on the skin is particularly striking in the complete prevention of the severe acrodynia accompanying pyridoxine deficiency in rats.[30]

Perhaps one of the greatest difficulties in ascertaining the essential nature of certain unsaturated fatty acids in human subjects may be attributed to the inability to measure accurately the content and distribution of linoleic and arachidonic acid in the blood and tissues. It is very striking, however, that changes in the pattern of the serum lipids are the same in human subjects as in experimental animals. Although by the bromination technic the tetrabromides and polybromides of serum were demonstrated to be reduced on a fat free diet, this cannot be taken as absolute evidence that the human subject has a special need for linoleic or arachidonic acid. This finding, however, together with various serum lipid studies, gives strong support to the theory that the human organism is unable to synthesize the unsaturated fatty acids which have been found to be essential for some animals. The adaptation of spectroscopic methods to the quantitative measurement of linoleic and arachidonic acids in human serum and tissue promises to aid further studies of the need for and the specific function of the essential fatty acids in human nutrition.

23. Epstein, N. N., and Glick, David: Unsaturated Fatty Acids in Eczema: Observations on Acne Vulgaris, Psoriasis, Xanthoma Tuberosum and Xanthoma Palpebrarum, Arch. Dermat. & Syph. **35:** 427 (March) 1937.

24. Taub, S. J., and Zakon, S. J.: The Use of Unsaturated Fatty Acids in the Treatment of Eczema (Atopic Dermatitis, Neurodermatitis), J. A. M. A. **105:** 1675 (Nov. 23) 1935.

25. Grulee, C. G., and Sanford, H. N.: The Influence of Breast and Artificial Feeding on Infantile Eczema, J. Pediat. **9:** 223, 1936.

26. Robinson, Edith C.: A Study of 240 Breast Fed and Artificially Fed Infants in the St. Louis Area: Incidence of Rashes and Gastrointestinal Disturbances in Breast Fed Infants and in Infants Fed on Fresh Milk Formulas and on Acidified (Lactic Acid) and on Nonacidified Evaporated Milk Formulas, Am. J. Dis. Child. **59:** 1002 (May) 1940.

27. Hilditch, T. P., and Meara, M. L.: Human Milk Fat: I. Component Fatty Acids, Biochem. J. **38:** 29, 1944; II. Component Glycerides, Ibid. **38:** 437, 1944.

28. Hansen, A. E., and Wiese, Hilda F.: Unpublished data.

29. Hansen, A. E., and Wiese, H. F.: Effect of Local Irritant on Skin of Dogs: Influence of Fat in Diet on Lipids of Serum and Tissues, Tr. Soc. Pediat. Res., Am. J. Dis. Child. **69:** 325 (May) 1945. Kooda, J.; Hansen, A. E., and Fredericks, M. G.: Effect of Local Irritant on Skin of Dogs: Influence of Fat in Diet, Fed. Proc. **3:** 91, 1944.

30. Salmon, W. D.: The Effect of Certain Oils in Alleviating Localized Erythematous Dermatitis (Acrodynia or Vitamin B_6 Deficiency) in Rats, Proc. Am. Soc. Biol. Chem., J. Biol. Chem. **123:** civ, 1938.

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SATURDAY, DECEMBER 7, 1946

ANTIBIOTICS AND THE CENTRAL NERVOUS SYSTEM

Rammelkamp and Keefer [1] demonstrated that penicillin does not pass through the blood-brain barrier in significant quantities following an intravenous injection of the substance. In normal subjects penicillin appeared to be slowly absorbed and slowly excreted in the urine following intrathecal injection of 5,000 or 10,000 Florey units. In subjects with meningitis, absorption of penicillin after intrathecal injection is more rapid than in normal persons. Injection of 10,000 Florey units in a normal volunteer was followed by headache, vomiting, increased intrathecal pressure and phagocytosis in the spinal fluid. After the injection of 5,000 Florey units, symptoms were not noted other than a slight headache and a slight increase in the number of leukocytes in the spinal fluid. In subjects with meningitis untoward symptoms were not noted following the injection of 10,000 Florey units. Sweet and his co-workers [2] recorded 2 instances of mild and 2 of severe sacral radiculitis following intrathecal injections of penicillin in 16 patients with pneumococcic meningitis. All these patients recovered. McCune and Evans [3] resorted to intraventricular injection of penicillin in a case of staphylococcic meningitis which did not respond to intravenous injections of sodium sulfadiazine and to repeated intrathecal injections of penicillin. A needle passed into the right ventricle of the brain yielded 8 cc. of slightly turbid, colorless fluid which showed only minimal bacteriostatic activity in spite of the fact that 7,500 units of penicillin had been introduced by lumbar puncture two hours earlier. Then 7,500 Florey units of penicillin was dissolved in 5 cc. of saline solution and introduced into the ventricle. There was no immediate reaction to the procedure. There was a definite improvement in the general condition of the patient, leading to complete recovery. These authors suggest that intraventricular use of penicillin may be resorted to as an adjunct to the intrathecal route of administration without untoward reactions and with good effect. A patient with Staphylococcus albus infection of the ventricular system was treated by Johnson and Walker [4] with 50,000 Oxford units by intraventricular injection. Within one hour the patient was comatose and in vascular collapse. For the next several hours he had clonic spasms of the arms, legs and neck. Within a day the patient appeared normal. Two days later 15,000 Oxford units of penicillin was injected into the right lateral ventricle. Four hours later the patient had twitchings of the right arm and leg which disappeared within a few hours. After further intraventricular injections of penicillin without reaction, the patient recovered completely.

Johnson and his co-workers [5] found that in the dog and the monkey approximately 500 Oxford units of penicillin applied to the cerebral cortex is sufficient to induce convulsive manifestations, which initially consist in chronic spasms of the contralateral extremities but later involve all the limbs in the manner of a generalized epileptic seizure. In man the convulsive threshold appears to be considerably higher. These toxic manifestations are not due to impurities in the penicillin, for pure crystalline penicillin induces the attacks. It appears from these experiments that penicillin when applied to the central nervous system in adequate amounts which, the authors stress, fortunately are far above therapeutic requirements, will induce convulsive manifestations which usually are of a temporary nature. These clinical fits are accompanied with the electroencephalographic manifestations which characterize epileptic attacks. Investigation of other antibiotics revealed that streptomycin applied to the central nervous system will induce mild convulsive manifestations of a temporary nature. The clinical and electroencephalographic manifestations are less severe than those produced by equivalent doses of penicillin. Streptothricin, actinomycin and clavacin, when directly applied to the central nervous system in large doses, likewise show convulsive propensities. Penicillin and streptomycin may be applied to the central nervous system without toxic effects in doses far above an adequate antibiotic concentration, whereas streptothricin, actinomycin and clavacin appear to produce severe toxic effects in concentrations little, if at all, above therapeutic levels. These antibiotic substances would

1. Rammelkamp, C. H., and Keefer, C. S.: The Absorption, Excretion and Toxicity of Penicillin Administered by Intrathecal Injection, Am. J. M. Sc. **205**: 342 (March) 1943.

2. Sweet, L. K.; Dumoff-Stanley, Edith; Dowling, H. F., and Lepper, M. H.: The Treatment of Pneumococcic Meningitis with Penicillin, J. A. M. A. **127**: 263 (Feb. 3) 1945.

3. McCune, W. S., and Evans, J. M.: Intraventricular Penicillin in the Treatment of Staphylococcic Meningitis, J. A. M. A. **125**: 705 (July 8) 1944.

4. Johnson, H. C., and Walker, A. E.: Intraventricular Penicillin, J. A. M. A. **127**: 217 (Jan. 27) 1945.

5. Johnson, H. C.; Walker, A. E.; Case, T. J., and Kollros, J. J.: Effects of Antibiotic Substances on the Central Nervous System, Arch. Neurol. & Psychiat. **56**: 184 (Aug.) 1946.

not be acceptable for clinical use in the central nervous system even if they were free from systemic toxic effects. As far as penicillin and streptomycin are concerned, the margin between the therapeutic concentration and the convulsive threshold is so great that with reasonable care the toxic effects should be avoidable.

CARDIAC DEPLETION ALLERGY

Study of the effects of bacterial toxins on the isolated vertebrate heart has led to the discovery of two types of cardiotoxins. The first type is illustrated by the action of Clostridium septicum toxin. Perfused through the isolated frog heart, this bacterial filtrate causes a progressive systolic and diastolic decrease. At the end of twenty minutes the ventricle usually stops beating midway between systole and diastole. A second type of cardiotoxin was recently described by Bernheimer and Cantoni [1] of the Departments of Bacteriology and Pharmacology, New York University College of Medicine. This type is illustrated by cardiotoxic filtrates from Streptococcus pyogenes and the type II pneumococcus.

In a typical experiment a dialyzed streptococcus filtrate was diluted twenty-five times with isotonic solution of three chlorides containing cysteine in a concentration of 1:1,000. The solution was administered by means of a Fühner cannula to an isolated frog heart and allowed to remain in the heart for twenty-three minutes. Even a suggestion of a toxic reaction was not recorded in the course of several hundred experiments. At the end of twenty-three minutes the solution was removed and the heart twice washed with the isotonic solution. A second dose of a toxic filtrate identical with the first was now introduced into the Fühner cannula. Within thirty seconds decreased relaxation of the ventricle occurred, increasing to a complete systolic contracture by the end of ninety seconds.

This toxicity cannot be explained as a result of summation of the two toxic doses. Control normal hearts tested with ten times the sum of the two doses did not show any suggestion of a systolic contracture. The phenomenon is apparently a true sensitization of the myocardium due to the initial contact with the dilute toxin. Similar sensitizations were demonstrated with type II pneumococcus filtrate and with preparations of Clostridium welchi theta toxin.

Analysis of this allergic phenomenon [2] shows that the myocardium, as a result of the initial contact with streptococcus filtrate, releases an inhibitory substance into the perfusion fluid in sufficient quantities to neutralize from five to ten times the routine toxic dose. Subsequent washings with isotonic solution of three chlorides remove nearly all of this toxin inhibitor. The depleted heart thus becomes hypersensitive to a second application of the same cardiotoxin.

Release of this toxin inhibitor was confirmed on mice. Intravenous injection of 0.5 cc. of a 1:25 dilution of streptococcus filtrate kills 16-20 Gm. mice within five minutes. Addition of from 0.125 to 0.5 cc. of inhibitor fluid from a perfused frog's heart usually prevents this toxic reaction completely, two third of all animals surviving indefinitely.

The toxin inhibitor is nondialyzable through a cellophane sac and is relatively heat stable, its inhibiting titer being only slightly reduced by heating to 100 C. for thirty minutes. The inhibitor is soluble in chloroform. By means of chloroform it can be extracted and recovered almost quantitatively from transfusion fluid. The stability of the inhibitor toward heat and its solubility in chloroform clearly set it apart from antibodies in the usual sense of the term.

From the point of view of immunologic theorists the local formation or release of inhibitor substances from the heart muscle is a most important addition to current theories of immunochemistry. Whether or not tissues other than the myocardium synthesize or release similar toxin inhibitors has not yet been determined.

1. Bernheimer, A. W., and Cantoni, G. L.: J. Exper. Med. **81**: 295 (March) 1945.
2. Cantoni, G. L., and Bernheimer, A. W.: J. Exper. Med. **81**: 307 (March) 1945.

"WETZEL'S GRIDS" IN PEDIATRIC ENGINEERING

Disease and its treatment, as Blackfan [1] pointed out, "are overshadowed by the problems of growth and development which . . . provide added duties for every physician who undertakes to furnish medical care for children—duties which in olden times were not required." None knew better than he the difficulties of these problems and the limitations of methods then available to deal with them. Now the Wetzel baby grid [2] as an introduction to pediatric engineering is conceived to be a practical method of surmounting the obstacles that have hindered physicians in judging the outcome of their efforts to promote sound growth.

This baby grid, which Wetzel describes as "a direct reading control chart on the quality of growth and development in individual infants," is an extension of principles and technic whose practical value in older children was recognized and commented on by THE JOURNAL [3] some years ago. More recently, in a significant critique contrasting the appraisal of human growth with the less complicated problem in cattle, Samuel Brody, student and investigator of bioenergetics and growth, remarked that "Wetzel gave the best expression to the weight-height-age status." The grid, accord-

1. Blackfan, Kenneth D.: Introduction to Pediatrics, in Brennemann's Practice of Pediatrics, Hagerstown, Md., W. F. Pryor Company, Inc., 1945, vol. 1, chapter 2, p. 1.
2. Wetzel, N. C.: The Baby Grid, J. Pediat. **29**: 439 (Oct.) 1946.
3. Physical Fitness from Two to Twenty, editorial, J. A. M. A. **116**: 1223 (March 22) 1941.

ing to Brody,[4] represents a "unique contribution . . . [which] brings together the weight, height, age and also metabolism data in one conveniently designed chart." There would seem to be good reason for physicians practicing pediatrics to look on the baby grid as Brody does on its forerunner.

The practical philosophy behind a baby grid is both interesting and instructive. Wetzel takes the point of view of an engineer confronted with the economic problem of controlling the quality of a factory's product where failure to do so would result in "going out of business."[5] He views the infant as the analogue of the factory, the infant's growth as the analogue of factory output. The aim in each case is to maintain "top quality" production and to know whether this is being done. In an infant, even in small premature babies, growth quality is directly gaged by the "fidelity" with which a baby conforms to the "tolerance limits" for speed and direction as patterned in the grid. Healthy infants exemplify, as Wetzel believes, a fundamental law that "growth is a moving and not a static function in babies." Those whose growth is faulty—the engineer's "rejects"—are identified by their departure from that law. As a further tie-in with the engineering approach, such matters as body surface, size and shape as well as energy requirements are also provided for in this one page compendium of infant growth. The physician can evaluate his data on a baby grid without indulging in the statistical pyrotechnics of other methods that are so oblivious to practical considerations as to require that a doctor manipulate sigmas, t-scores or similar paraphernalia of investigative research.

By coincidence the baby grid appears as the American Academy of Pediatrics is in the midst of its earnest, forward looking study of child health services.[6] While these efforts are more immediately concerned with gathering factual data for scientific planning of postwar infant and child care, the ultimate results will sooner or later affect millions of children whose natural right is the opportunity to achieve "top quality growth." But that result, as Wetzel shows, "presumes knowledge on how well a given baby is fulfilling its own capacity for growth." The engineering equipment required for this particular job seems now to be at hand in the form of the baby grid. Pediatricians will utilize this simple precision instrument as an aid in their work with babies, just as the American Association of Teachers Colleges has found the "big grid" useful in their own new curricular emphasis on the growth of school children.[7]

4. Brody, Samuel: Bioenergetics and Growth, New York, Reinhold Publishing Corporation, 1945, pp. 638 and 639.

5. Wetzel, N. C.: Mass, Volume, Surface and Energy Relationships in Human Growth and their Application to the Problem of Growth Failure in Children, Cleveland Engineering **39**: 5 (March 7) 1946.

6. The American Academy of Pediatrics Study of Child Health Services, editorial, J. A. M. A. **131**: 32 (May 4) 1946.

7. Child Growth and Development Emphases in Teacher Education, Prepared by the 1943-1944 Teachers College Collaborators, Lonzo Jones, Chairman, American Association of Teachers Colleges, p. 23.

Current Comment

ENVIRONMENT AND PHYSIQUE

The relation between environment in the broad sense and the physical development of human beings has been the subject of many scientific studies and much speculation. Recently Lasker[1] made physical measurements on 284 adult Chinese, 97 of whom were Cantonese immigrants, 48 American born Chinese of Cantonese extraction, 5 Hawaiian born Chinese, 9 Cantonese born elsewhere and the remainder from other parts of China. The standard methods of examination described by Martin[2] were followed, with a few exceptions. Certain differences in physique of Chinese men born and raised in the United States were found as compared with Chinese immigrants born in China. These differences included an increase in the stature and in all the measurements correlated with stature, such as trunk and limbs, other than chest depth. The thoracic, brachial, hand and foot indexes tended to be lower in the Chinese of American birth. The American born Chinese had wider and shorter heads and longer, narrower, higher noses and longer faces. Lasker concluded that the typical oriental youth brought up or born in the United States or Hawaii differed from immigrants of like stock in what he calls an "environmental growth factor." The former is taller with longer arms and legs, relatively smaller hands and feet and flatter chest. His head is likely to be shorter but broader and the nose relatively narrower. More body hair is in evidence. The changes noted in the Chinese born in the United States seem to reflect a process caused by changed diet or other factors incident to the migration of peoples. Whether such physical changes as exist are due primarily to diet, to climate or to other environmental factors would be interesting to investigate though extremely difficult to determine.

THE EYE BANK

The Eye Bank for Sight Restoration, Inc., established in 1944 in New York City, was conceived as a centralized agency where eyes could be systematically salvaged, preserved and redistributed to doctors who perform the corneal grafting operation. Originally twenty leading ophthalmologists in key cities throughout the country acted as advisers and interpreters of the program. At present over two hundred and thirty-seven doctors are serving throughout the nation. To the initial twenty-two prominent New York hospitals that participated in the project at its inception there have been added fifty-six hospitals throughout the country. Transportation for incoming and outgoing eye material has been made available through the cooperation of the American Red Cross and various airlines. In addition to supplying corneas for surgical procedures, the eye bank has carried on a widespread program of education both of the public and of physicians through the press, magazines, the radio and the distribution of literature. During the first year of activity nine

1. Lasker, Gabriel Ward: Migration and Physical Differentiation, Am. J. Phys. Anthrop. **4**: 273 (Sept.) 1946.

2. Martin, Rudolf: Lehrbuch der Anthropologie, ed. 2, Jena 1928.

scholarships were awarded to ophthalmologists, who, after their training, will return to states throughout the country to be associated with medical centers. In addition, two fellowships have been granted. The facilities of the Ayer Laboratory for Corneal Research have been made available for routine and investigative work. Here the eyes are received, given a prompt and careful examination to determine the condition of the corneal tissue, put under a twenty-four hour culture test and then sent with directions to doctors for grafting operations. After the corneal tissue has been used the eyes receive a pathologic examination, and the results of this are reported to the hospital or doctor whence the eyes originated. Challenging research problems which have been attacked include studies on corneal preservation, technics of transplanting the vitreous humor and investigations of the metabolic and histologic properties of the eye. An information kit of educational material may be obtained by writing to the Eye Bank for Sight Restoration, Inc., 210 East 64th Street, New York 21.

VACCINATION FOR MUMPS

Active attempts are now being made to develop a satisfactory vaccine against mumps. Recently Stokes and his colleagues [1] reported on the use of formol-inactivated suspension of mumps virus as a vaccine against mumps. Four groups of children were studied who were inmates of three institutions. A negative complement fixation test was the only criterion of susceptibility in the selection of the first two groups. In the third group this test was used and also, as a further check on susceptibility, skin tests. The fourth group consisted of those who at the beginning of the experiment were found to be negative both by complement fixation and by skin test. In the first, second and fourth groups approximately half of the children were given suspension of mumps virus inactivated by the addition of formol. The remaining children were controls. In the third group about two thirds of the children were vaccinated. The vaccine was administered in the first, second and fourth groups by a subcutaneous route in two doses each of 0.3 cc. of a 10 per cent and of 0.5 cc. of the 2.5 per cent suspension at an interval of five days. The period for testing the vaccinated group was fourteen to seventeen days from the date of first injection of the vaccine. The virus employed in testing the efficacy of vaccination was introduced by injection directly into Stensen's duct or by spray. A variable degree of swelling of the inoculated parotid gland appeared after the injection of virus in all of those who received the virus by direct inoculation. However, the interval between the inoculation with live virus and the time at which the maximal enlargement of the gland was noted varied considerably in the vaccinated and the control groups. About four fifths of the vaccinated may be considered to have exhibited evidence of resistance as compared with about one fourth of the controls. The principal conclusion from the study was that vaccination with formol inactivated virus apparently leads to increased resistance in about half of the children whose immunologic status was subsequently tested by experimental inoculation of pathogenic material. The degree of protection in human beings afforded by the formolized vaccine is therefore of about the same degree as that observed in monkeys vaccinated in the same manner.

1. Stokes, Joseph, Jr., and others: Immunity in Mumps: VI. Experiments in the Vaccination of Human Beings with Formolized Mumps Virus, J. Exper. Med. **84:** 407 (Nov.) 1946.

PHYSIOLOGIC STANDARDS IN ADOLESCENCE

Pediatrics has been well established for many years; geriatrics is making a bid for recognition; specialty practice outside the pediatric and geriatric age groups is concerned with adult patients. There remains, however, a special age group which has peculiar physiologic, pathologic and psychologic problems. Significant studies are now appearing regarding these important medical factors in adolescence.[1] Among these the surveys made by Nathan W. Shock [2] are particularly important. These studies were initiated by the Institute of Child Welfare at the University of California and have been continued under the direction of the National Institute of Health. Shock emphasizes the difficulty of establishing adequate standards for physiologic factors in adolescence. Shuttleworth [3] in 1938 demonstrated the serious limitations of average values usually regarded as "age norms" obtained from averages of different children measured at successive ages. Repeated measurements on the same children during growth have shown the individuality of the growth process. Shock emphasizes that the rapidly maturing adolescent may find himself in difficulties because adults expect from him behavior or performance consistent with his size. Since size and social or intellectual maturity do not necessarily proceed together, it often happens that the "large" adolescent is relatively immature. Thus he may be unable to meet the expectations of adults with respect to performance or behavior. The failure to "deliver" in the eyes of his peers or of adults is not an uncommon source of psychologic tensions. Probably inadequacy felt or observed by many adolescents has a definite physical or physiologic basis, but the nature of the factors concerned may vary widely among different boys and girls. Knowledge of individual differences in rates of maturing, as illustrated by the observations reported by Shock, can do much to minimize the emphasis placed all too often by school physicians and councilors on attaining "normal" values. The pediatrician is in a strategic position to aid developing adolescents in understanding and evaluating their own development.

1. Jones, H. E.: Development in Adolescence, New York, D. Appleton-Century Company, 1943. Stolz, H. R., and Stolz, L. M.: Adolescent Problems Related to Somatic Variations, Nat. Soc. Study Educ., 43d Yearbook, part I, 1944, p. 80.

2. Shock, N. W.: Age Changes and Sex Differences in Alveolar CO_2 Tension, Am. J. Physiol. **133:** 610 (July) 1941; Standard Values for Basal Oxygen Consumption in Adolescents, Am. J. Dis. Child. **64:** 19 (July) 1942; The Effect of Menarche on Basal Physiological Functions in Girls, Am. J. Physiol. **139:** 288 (June) 1943; Physiological Changes in Adolescents, Nat. Soc. Study Educ., 43d Yearbook, part I, 1944, p. 56; Basal Blood Pressure and Pulse Rate in Adolescents, Am. J. Dis. Child. **68:** 16 (July) 1944. Shock, N. W., and Soley, M. H.: Average Values for Basal Respiratory Functions in Adolescents and Adults, J. Nutrition **18:** 143 (Aug.) 1939. Shock, N. W.: Some Physiological Aspects of Adolescence, Texas Rep. Biol. & Med. **4:** 289-309, 1946.

3. Shuttleworth, F. K.: Sexual Maturation and the Skeletal Growth of Girls Age Six to Nineteen, Monogro. Soc. Res. Child Develop. **3:** 1, 1938.

ORGANIZATION SECTION

Official Notes

RESOLUTIONS TO BE PRESENTED TO HOUSE OF DELEGATES

The following resolution will be presented to the House of Delegates at the Supplemental Session, December 9 to 11, by the Indiana delegation:

Resolution on National Conference of County Medical Society Officers

WHEREAS, Public relations, as pertains to organized medicine, has a most important field of effort in reaching and giving information to and receiving suggestions from the rank and file of doctors who give medical service to the public the country over; and

WHEREAS, Efforts in this direction have been so successfully carried on by the secretaries' conferences sponsored by several of the state medical societies; and

WHEREAS, There is no national group at present functioning in this capacity; therefore be it

Resolved, That the American Medical Association sponsor a national conference of officers of county medical societies which shall meet yearly just preceding the annual session of the House of Delegates of the American Medical Association for the purpose of bringing to the annual session the diverse problems of the various localities, the exchange of ideas which would be helpful to the state conferences, in such matters as voluntary health insurance plans, hospitalization plans, construction of new hospitals in needed places, and improvement in medical facilities, rural health activities, nursing activities and the activities of the various Councils of the American Medical Association.

Dr. E. Vincent Askey, delegate of the California Medical Association, will present the following resolution:

Resolution on Requirements for Approval of Hospitals

WHEREAS, The problem of hospitalization is urgent now and will be distressingly difficult for an indefinite period of time; and

WHEREAS, There is apparently a definite plan to limit staff membership in hospitals to diplomates of the various specialty boards; and

WHEREAS, The limiting of staff memberships and heads of departments of such staffs in hospitals to such diplomates could tend to injure the best interests of the public and the medical profession as a whole; and

WHEREAS, Of a total of 180,000 physicians in the United States approximately only 22,000 are diplomates of all specialty boards, and limitation by the hospitals of their facilities to use by these few would work an injustice on other capable doctors and their patients; therefore be it

Resolved, That the House of Delegates of the American Medical Association suggests to the Council on Medical Education and Hospitals and directs it to further the realization of this suggestion, to wit:

The requirements for approval of hospitals shall be so defined that there shall be (1) adequate protection of the rights of all doctors and their patients in obtaining hospitalization to the end that general practitioners as well as specialists shall have access to and use of hospital facilities; (2) that the criterion of whether a doctor may be a member of a staff or head of a department shall be his actual ability as a doctor and not dependent on special society or board membership, and (3) that the American College of Surgeons be urged to conform to these general policies in its procedures in the standardization of hospitals.

Coming Medical Meetings

American Medical Association House of Delegates Supplemental Session, Chicago, Dec. 9-11. Dr. George F. Lull, 535 N. Dearborn St., Chicago 10, Secretary.

Conference of State Secretaries and Editors, Chicago, Dec. 7-8. Dr. George F. Lull, 535 N. Dearborn St., Chicago 10, Secretary.

American Academy of Dermatology and Syphilology, Cleveland, Dec. 7-12. Dr. Earl D. Osborne, 471 Delaware Ave., Buffalo, N. Y., Secretary.

American College of Surgeons, Cleveland, Dec. 16-20. Dr. Dallas B. Phemister, 40 E. Erie St., Chicago 11, Secretary.

American Society of Anesthesiologists, New York, Dec. 12. Dr. Curtiss B. Hickcox, 745 Fifth Ave., Room 1503, New York, Secretary.

Puerto Rico, Medical Association of, Santurce, Dec. 13-15. Dr. Rafael A. Vilar, P. O. Box 3866, Santurce, Secretary.

Southeastern Allergy Association, Atlanta, Ga., Jan. 18-19. Dr. Katharine B. MacInnis, 1515 Bull St., Columbia 49, S. C., Secretary.

Southern Surgical Association, Hot Springs, Va., Dec. 10-12. Dr. Alfred Blalock, Johns Hopkins Hospital, Baltimore 5, Secretary.

Washington Letter

(From a Special Correspondent)

Dec. 2, 1946.

Insulin Increased 50 Per Cent in Price Without Price Control

Increases of 50 per cent in the price of insulin are reported by producers, following the removal of price controls here. Eli Lilly and Company of Indianapolis has announced an increase of this amount and the other manufacturers are reported to be following suit. The drug is a necessity to around a million diabetic sufferers in this country. Industry spokesmen say that the rise in price is necessary because of the increased demand for beef and pork pancreas glands, the raw material for insulin, and because of new uses for insulin as well. The glands also have new uses in protein extracts for supplemental diseases. Insulin was for long under close price control.

Medical Center May Be Patterned After Massachusetts General Hospital

The $20 million hospital center to be erected in the nation's capital may be patterned after the Massachusetts General Hospital in Boston, which has separate medical and surgery buildings, is erecting a building for women's diseases, has two private patient buildings on luxury and middle income levels, and operates separate institutions for mental patients and tumor research and treatment. The three Washington hospitals involved in the Washington center may have functions allocated as follows: Emergency, devoted to surgery; Garfield, devoted to medicine, and Episcopal Eye, Ear and Throat continuing present specialized services. Emergency and Garfield hospitals must continue as separate entities to keep endowments and present operating funds.

Cancer Society Incorporates District of Columbia Division

Dr. H. H. Kerr, president of the newly incorporated District of Columbia Division of the American Cancer Society, said that the group plans a "really effective cancer control program." Washington's first organized program against cancer will be preceded by a survey of cancer needs to be paid for by the U. S. Public Health Service. The survey director will be chosen by District Health Officer Ruhland from a list of experts compiled by Dr. Calvin T. Klopp, director of the Warwick Memorial Cancer Clinic in Garfield Hospital.

Psychiatric Foundation Organized

Following the example of tuberculosis, cancer and infantile paralysis movements, the Psychiatric Foundation, a nonprofit corporation, has been formed to fight mental illness. The foundation is composed of laymen and specialists. The group has the endorsement of the American Psychiatric Association, the American Neurological Society and the National Organization of Public Health Nursing.

Walter Reed Hospital Faces Cuts in Funds and Personnel

The economy program of the Army is expected to cause further cuts in budget and personnel of Walter Reed Hospital, although both categories have already been reduced by about 25 per cent, it is reported. There is not expected to be a reduction in the patient load at the hospital because temporary hospitals throughout the country are being closed and some of their patients are coming to Walter Reed.

Predicted Influenza Epidemic Is Slow in Arriving

The U. S. Public Health Service has indicated that a predicted influenza epidemic is slow in materializing. There were 2,104 cases throughout the nation for the week ended November 16, which is about half the number of cases reported for the same week last year. Of the recent total Texas reported 1,039, Virginia 317, North Carolina 309 and Arizona 130.

GOVERNMENT SERVICES

ARMY

29TH GENERAL HOSPITAL (THE COLORADO UNIT) SCHEDULED FOR INACTIVATION

The 29th General Hospital, chief army medical installation in southern Korea, will be inactivated before December 15. Activated as a 1,000 bed general hospital on Sept. 1, 1942 at Fort George Meade, Maryland, this hospital drew its professional personnel from the University of Colorado School of Medicine, Denver. The unit arrived at New Caledonia on Nov. 21, 1943, and more than 12,000 casualties from Bougainville, Munda, Saipan, Leyte, Peleliu and other South Pacific campaigns were treated at this hospital. In April 1945 the unit was ordered to Okinawa and in October of that year to Seoul, Korea. The hospital has given general hospital type care to members of the occupation in Korea since then.

The commanding officer of the 29th General Hospital while in the South Pacific was Col. William C. Pollack. Lieut. Col. John M. Foster was in command from July 5, 1944 to November 1945 and Col. Jonathan M. Rigdon from December 1945 to July 1946. From August to September 1946 Major Harold V. Ellingson, Cleveland, who is still with the hospital, was in command. The present commanding officer is Lieut. Col. William B. Stryker of St. Paul.

The hospital was awarded the Army Meritorious Service Unit Plaque July 30 of this year for superior performance of duty in the execution of exceptionally difficult tasks in New Caledonia from January to April 17, 1945.

MEETING AT 42D GENERAL HOSPITAL IN JAPAN

About 150 army doctors of the Tokyo-Yokohama area held the regular bimonthly meeting November 13 at the 42d General Hospital. Addresses were given by Col. C. L. Gandy, Ocean View, N. J., commanding officer, 42d General Hospital; Col. P. L. Cook, Wyalusing, Pa., surgeon, Eighth Army; Brig. Gen. J. A. Bethea, U. S. Army, Marion, S. C., chief surgeon, A. F. P. A. C.; Capt. M. H. Paushter, Springfield, Mass., on Methyl Alcohol Poisoning; Capt. M. C. Blanchard, Columbus, Ga., Infectious Mononucleosis; 1st Lieut. Edmunds G. Dimond, Indianapolis, Mediastinal Emphysema; 1st Lieut. Alan Davidson, St. Albans, Vt., Management of Foreign Bodies in the Eye; Capt. G. O. Wellman, Hurricane, W. Va., Gunshot Wounds of the Abdomen and Rupture of the Liver; 1st Lieut. Walter J. Wilkins, Poplar Bluff, Ark., Rupture of the Duodenum; Capt. Donald E. Preshaw, Detroit, Atelectasis with Pleural Effusion; Capt. Chester B. Powell, Chicago, Management of Head Injuries; Capt. Thomas H. Williams Jr., Montgomery, Ala., Management of Injuries to the Genitourinary Tract, and 1st Lieut. H. I. Posin, New York, of the 361st Station Hospital, Epilepsy.

PROFESSIONAL ACTIVITIES AT HALLORAN GENERAL HOSPITAL

A special week of professional activities began at U. S. Halloran General Hospital, Staten Island, New York, on November 18. Following a series of rounds in the Dermatology and Medical buildings and clinics in orthopedic and neurosurgery, a conference was addressed by Dr. Harry Gold, associate professor of pharmacology, Cornell University Medical College, on treatment of cardiac failure. At a conference on the following day, with clinics and rounds, Dr. Hirsh Liebowitz, instructor of medicine, New York University College of Medicine, discussed the treatment of peptic ulcer. A film on bronchial asthma was presented and a symposium on preoperative orthopedics. Other activities during the week comprised a cardiac fluoroscopy clinic, rounds in general surgery and postoperative neurosurgery and orthopedic postoperative evaluation, all under the general supervision of Col. O. H. Stanley, M. C., U. S. Army, commanding officer of the hospital.

GENERAL KIRK AWARDED CROSS OF LEGION OF HONOR

Major Gen. Norman T. Kirk, the Surgeon General of the United States Army, was recently awarded the Cross of the Legion of Honor in the degree of Commander at the office of the French military attaché, Washington, D. C. In the same ceremony the degree of Chevalier was awarded to Brig. Gen. Raymond W. Bliss, Deputy Surgeon General of the United States Army. The presentations were made by the Surgeon General of the French army, Gen. Raymond Debenedetti, who was accompanied by Col. Alexander Ribollet and Major Pascaul Santini, French staff officers.

ARMY AWARDS AND COMMENDATIONS

Brigadier General Robert M. Hardaway

The Legion of Merit was recently awarded to Brig. Gen. Robert M. Hardaway, M. C., U. S. Army, of Washington, D. C., "for exceptionally meritorious service as commanding general, Bushnell General Hospital, from August 1942 to January 1946. General Hardaway's sound foresight and effective planning" was credited in the citation as resulting "in the highest type medical and surgical treatment for all patients. He developed a superior program for amputee patients throughout the Ninth Service Command. Through extensive professional knowledge, initiative and unremitting devotion to duty, he provided these patients with a highly efficient method for training in the use of artificial limbs." Dr. Hardaway graduated from Washington University School of Medicine, St. Louis, and entered the service May 25, 1912.

Colonel Charles T. Young

The Oak Leaf Cluster to the Legion of Merit was recently awarded to Col. Charles T. Young, M. C., U. S. Army, of Washington, D. C., for meritorious service from March to October 1945 as commanding officer, Wakeman Convalescent Hospital, where "he displayed a high type of organizational ability and leadership." The citation also states that "by reason of his judgment, energy and superior force and leadership Colonel Young was responsible for the outstanding qualities of Wakeman Convalescent Hospital, and contributed materially to the war effort." Dr. Young graduated from John Hopkins University School of Medicine and entered the service Aug. 3, 1928.

Lieutenant Colonel Weldon K. Ruth

The Bronze Star was recently awarded to Lieut. Col. Weldon K. Ruth, M. C., U. S. Army, of O'Keene, Okla., who "performed meritorious and heroic services from April 10 to 22, 1942 during the march of captured Americans from Bataan Province to Japanese concentration camp near Capas, Tarlac, Philippine Islands." Lieutenant Colonel Weldon was cited for disregarding his own condition and risking brutalities and death at the hands of the Japanese by continually attending his sick, exhausted comrades. "He prevented the murder of two officers on separate occasions by interposing his body between them and enemy soldiers until he could revive them enough to continue the march. Major Ruth's ministrations did much to alleviate the suffering of his fellow prisoners of war." Dr. Ruth graduated from the University of Oklahoma School of Medicine, Oklahoma City and entered the service Dec. 7, 1936.

NAVY

ADMIRAL SWANSON TO SUCCEED ADMIRAL McINTIRE AS SURGEON GENERAL

President Truman on November 27 appointed Capt. Clifford A. Swanson Surgeon General of the Navy and chief of the Bureau of Medicine and Surgery, with the rank of Rear Admiral. Admiral Swanson, whose selection is a recess appointment pending confirmation by the Senate, will succeed Vice Admiral Ross T. McIntire, who has held that position since his appointment by President Roosevelt on Dec. 1, 1938. Admiral Swanson is from Marquette, Mich., and graduated from the University of Michigan Medical School, Ann Arbor, in 1925. He is a member of the American Academy of Ophthalmology and Otolaryngology and has been certified by the American Board of Otolaryngology. He entered the medical corps of the Navy in June 1925.

Admiral McIntire, a native of Oregon, graduated in medicine in 1912 from the Medical School of Willamette University, now the University of Oregon School of Medicine. He was the first Surgeon General of the Navy to be born west of the Rocky Mountains. In addition to the duties of Surgeon General and chief of the Bureau of Medicine and Surgery, he served also as White House physician. His present appointment expired November 1. Mr. Truman provided that Admiral McIntire will retain the rank of Vice Admiral when detached from his present duties. Admiral McIntire was also a specialist in ophthalmology and otolaryngology. He is due to retire in a short time, when he will have completed thirty years of active duty in the Navy.

NAVY AWARDS AND COMMENDATIONS

Captain Frederick L. McDaniel

The Commendation Ribbon was recently awarded to Capt. Frederick L. McDaniel (MC), U.S.N., "for conspicuous and outstanding service as senior medical officer of the U. S. S. *Benevolence* when that hospital ship was suddenly and without forewarning called on to screen, treat and otherwise care for the first 1,500 Allied prisoners of war released from Japanese prison camps in the Tokyo Bay area. Subsequently," continues the citation, "under his able professional supervision the many hundreds of seriously ill American prisoners of war were afforded the highest type of medical skill and treated with most meticulous and kindly service. The quality of leadership demonstrated by Captain McDaniel was an inspiration to his staff associates and a reassurance to the suffering prisoners of war. His conduct was at all times in keeping with the highest traditions of the United States Naval Service." Dr. McDaniel graduated from the University of Maryland School of Medicine in 1913 and entered the service in May 1917.

PERSONAL

The Bureau of Medicine and Surgery announced the assignment of Commander James A. Grindell (MC), U.S.N., to the Massachusetts General Hospital, Boston, for a course in cardiology.

PUBLIC HEALTH SERVICE

FELLOWSHIPS IN HEALTH EDUCATION

Fellowships leading to a Master's Degree in Public Health in the field of Health Education are being offered to any qualified United States citizen between the ages of 22 and 40, according to a statement by the U. S. Public Health Service. Tuition, travel expenses for field training and a stipend of $100 a month will be provided out of funds furnished by the National Foundation for Infantile Paralysis. Candidates must hold a bachelor's degree from a recognized school and must be able to meet the entrance requirements of the accredited school of public health of their choice. In addition, courses in the biologic sciences, sociology and education may be required. Training in public speaking, journalism, psychology and work in public health or a related field are considered desirable qualifications.

The year's training, which begins with the 1947 fall term, consists of eight or nine months' academic work including public health administration, epidemiology, public health and school education, problems in health education, community organization and information technics and three months of supervised field experience in community health education activities. Application blanks may be obtained by writing the Surgeon General, United States Public Health Service, Washington 25, D. C., and must be filed prior to March 15, 1947.

Veterans are encouraged to apply and will be paid the difference between their subsistence allowance under the G. I. Bill of Rights and the monthly stipend of $100. Employees of local and state health departments are not eligible, since federal grants-in-aid are already available for such training purposes.

GRANTS FOR CANCER RESEARCH

The U. S. Public Health Service has announced that grants-in-aid amounting to about $200,000 have been recommended by the National Advisory Cancer Council for the support of cancer research projects in twenty-one universities, hospitals and research institutions. The variety of projects covered by the grants illustrate the complexity of the cancer problem and the many angles from which research must be carried on to solve it. The grants were recommended at the thirty-second meeting of the council held November 8 at the National Cancer Institute, Bethesda, Md., and presided over by Dr. James A. Crabtree, Acting Surgeon General, U. S. Public Health Service. The members of the National Advisory Cancer Council are Dr. Thomas Parran, Surgeon General, U. S. Public Health Service, who is chairman ex officio and in whose absence Dr. Crabtree presided; Dr. George M. Smith of Yale University, executive director of the council; Dr. Frank E. Adair, president of the American Cancer Society, New York City; Dr. A. C. Ivy, acting dean, University of Illinois Medical School, Chicago; Dr. Charles B. Huggins, professor of surgery, University of Chicago School of Medicine, Chicago; Dr. Sherwood Moore, director of the Mallinckrodt Institute of Radiology, Washington University, St. Louis, and Dr. Robert S. Stone, professor of radiology, University of California Medical School, San Francisco.

NEW ASSISTANT CHIEF, BUREAU OF STATE SERVICES

Dr. Herman Hilleboe has been appointed to the newly created post of assistant chief, Bureau of State Services, United States Public Health Service. Dr. Hilleboe will continue to discharge his regular duties as chief of the Tuberculosis Control Division. A graduate of the University of Minnesota Medical School and of the School of Public Health at Johns Hopkins University, he has been in public health activities since 1933, when he was appointed director of the Minnesota State Division of Tuberculosis Control. In 1937 he became special consultant in tuberculosis to the National Institute of Health and in 1939 became senior assistant surgeon in the Regular Corps of the Public Health Service. He was appointed by the Secretary of State to attend the fourth World Conference of Workers for Crippled Children in London, England, and, while abroad, inspected tuberculosis control programs in England, Germany, France and the Scandinavian countries. In 1942 Dr. Hilleboe was assigned to duty in the Public Health Service and made medical officer in charge of the Tuberculosis Control Section, States Relations Division. In 1944 he was appointed chief of the newly created Tuberculosis Control Division, with the rank of medical director.

VETERANS ADMINISTRATION

THE HOME TOWN MEDICAL CARE PROGRAM

Dr. Paul R. Hawley, medical director of the Veterans Administration, explained on November 14 the extent of the medical services which may be rendered to veterans under the home town medical care program. Existing legislation provides that veterans may be furnished outpatient medical or dental treatment in VA clinics, in private offices of physicians or dentists, or in their own home *only for disabilities recognized by VA as incurred or aggravated in line of duty in active service.* Only prescriptions for service connected disabilities may be filled at government expense by local pharmacies under VA's home town prescription service. The medical facilities of VA regional and subregional offices, clinics and hospitals under law must be utilized to the fullest extent for examination and outpatient treatment of veterans. When it has to be determined whether a veteran residing in an area where there is a VA field station (such as a clinic or a hospital) is to be referred to a VA clinic or to a civilian physician, the best interest of both the veteran and the government will be considered.

If veterans establish to the satisfaction of the chief medical officer of a VA regional office that reporting to a field station would work unnecessary physical hardship or cause excessive loss of time from employment, fee-basis doctors may be utilized. In any event, final decision rests with chief medical officers of VA regional offices. Then too, when the backlog of physical examinations justifies or when outpatient treatment is not being rendered expeditiously, the chief medical officers of VA regional offices may utilize the services of civilian physicians working under statewide contracts with the Veterans Administration.

Male veterans may be admitted to private hospitals (preferably those under contract by VA) for inpatient treatment of service connected disabilities by civilian physicians under contract to VA only if their condition is such as to constitute an emergency which cannot be met by a VA hospital because of the lack of beds or because the patient's condition prohibits travel. Prior authorization for this hospitalization and treatment in a private hospital must be obtained. If, owing to the extreme emergency of the case, prior authorization is not obtained, the physician or admitting hospital should notify VA within seventy-two hours. If the facts so warrant, VA will issue authority for the veterans's private hospitalization and treatment. Women war veterans may be admitted to private hospitals (preferably those under contract by VA) for inpatient treatment of *both service connected and non-service connected disabilities* by civilian physicians if it is an emergency which cannot be met by VA or because of the unavailability of beds or because the serious condition of the patient precludes travel. Authorization must be obtained exactly as in the case of male veterans.

CONTRACT WITH WEST VIRGINIA MEDICAL ASSOCIATION

Dr. Andrew E. Amick, president of the West Virginia State Medical Association, has appointed a board of review under the provisions of the contract between the association and the Veterans Administration. The board is composed of Drs. Claude B. Smith and Paul H. Revercomb of Charleston and James R. Brown of Huntington. The board will review reports which are deemed by the Veterans Administration to be inadequate or which do not meet the requirements of the Veterans Administration, recommend, at its discretion, the disqualification of any physician from further work with the Veterans Administration whose work is found by the board to be unsatisfactory, and advise and assist the Veterans Administration in other matters within the scope of the program.

With the signing of the contract the work of the Veterans Affairs Committee was completed. This committee, which has functioned since early in the year, was composed of Drs. Claude B. Smith, Charleston, chairman; C. O. Post, Clarksburg; Thomas L. Harris, Parkersburg; Francis A. Scott, Huntington, and Ralph J. Jones, Charleston. As of November 15, 809 members of the West Virginia State Medical Association have been certified as fee designated physicians under the veterans care program.

SPECIAL ORTHOPEDIC SHOES FOR VETERANS

Veterans with service connected disabilities now may obtain special orthopedic shoes free of charge from the Veterans Administration. Machines to make plaster casts of injured or deformed feet have been transferred from the War Department to the Veterans Administration and two are already in operation at the VA hospital, Hines, Ill., and the VA hospital at Atlanta, Ga., formerly the Army's Lawson General Hospital. Machines will be installed later at VA regional offices in Kansas City, Mo., New York and San Francisco. Plaster casts made by these machines will be sent to the army's quartermaster supply depot at Boston, where special lasts and patterns will be developed. The orthopedic shoes then will be constructed by commercial contractors, and completed shoes will be shipped to veterans by the VA regional office or hospital making the purchase.

Qualified veterans and also army personnel will be eligible for the service at establishments where the cast-making machines are in operation. Veterans should make applications through their nearest VA representative.

Cast-making machines are maintained by the Army at the Orthopedic Footwear Clinic, Boston, Walter Reed General Hospital, Brooke Army Medical Center, Fort Sam Houston, Texas, Fitzsimons General Hospital, Denver, and Madigan General Hospital, Fort Lewis, Washington.

PSYCHIATRISTS WANTED

Psychiatrists, clinical psychologists and psychiatric and medicosocial workers are needed by the Veterans Administration to serve in VA mental hygiene clinics now being operated in twenty-three cities. Twenty or more additional clinics in other cities are to be opened when personnel to staff them is available. Minimum qualifications for psychiatrists require certification as specialists by the American Board of Psychiatry and Neurology, or eligibility for the examination.

The grade of a psychiatrist is determined by professional qualifications, and base pay per year ranges from $4,149.60 to $10,000. Certification by the American Board of Psychiatry and Neurology entitles the psychiatrist to an additional 25 per cent of the base salary up to a limit of $11,000.

Positions for clinical psychologists and psychiatric and medicosocial workers are under the rules and regulations of the U. S. Civil Service Commission. The base pay per year ranges from $4,149.60 to $6,862.80. Applicants must have at least two years of progressively responsible experience in the application or teaching of psychologic principles and technics and proved ability to evaluate personality problems. In addition, all candidates must have completed ten required courses in the field of psychology. If an applicant has completed all requirements for a doctor's degree in psychology, he will be accepted as meeting this education requirement.

Social workers (psychiatric and medical) earn from $3,397.20 to $5,905.20 per year. One year of training in an approved school of social work is the minimum educational requirement for these positions. This training must have included supervised field work and courses in psychiatric or medical information plus the required experience, which is one year in a health or welfare agency of acceptable standards. Additional qualifying experience is required for higher grade positions. Applicants may substitute one year of training (in addition to that used to satisfy the basic requirement) completed in an approved school of social work for one year of experience.

Veterans Administration mental hygiene clinics now in operation are located at Boston, Denver, Des Moines, Iowa, St. Louis, Los Angeles, Baltimore, Pittsburgh, Chicago, Newark, N. J.,

New Orleans, Cleveland, Cincinnati, Detroit, Minneapolis, Portland, Ore., San Francisco, Seattle, Providence, R. I., Milwaukee, Hartford, Conn., Dallas, Texas, Philadelphia and Washington, D. C.

VETERANS' CARE IN CONNECTICUT

Connecticut's "home town" medical care plan for war veterans with service connected illnesses or injuries has been approved by the Veterans Administration. The Connecticut State Medical Society plan is now being put into action through a broad educational program among its more than 2,200 members. Main emphasis of the plan is directed toward the development of medical care for veterans in their own communities "to cultivate wholesome physician-patient relationships" and "100 per cent participation" in the plan by physicians throughout the state.

Four veteran medical officers, all members of the society, comprised the committee which developed the plan. They are Dr. Samuel B. Rentsch, chairman, of Derby, Dr. Egbert M. Andrews of Hartford and Drs. Norton Canfield and Joseph N. D'Esopo of New Haven.

MISCELLANEOUS

BANDAGES AND DRESSING FOR SALE

The War Assets Administration announces that large quantities of all types of surgical bandages and dressings which cost the government more than $1,000,000 will be offered to priority and other eligible buyers from November 20 to December 10. WAA Regional Offices at Denver, Kansas City, Mo., New York City, San Francisco and Seattle are conducting the fixed price sales. Detailed descriptions, prices and minimum purchase requirements may be obtained by writing any of the five regional offices handling the disposal.

More than 250,000 triangular compressed bandages and about 300,000 gauze bandages, some 3 inches and others 4 inches wide and all 6 yards long, are included in these sales. Large quantities of white gauze roller bandages, 4 inches by 10 yards, packed twelve rolls to a box, and of compressed bandage gauze, 3 inches by 6 yards, packed seventy-two to a box, are available at some of the five regional offices.

Orders will be accepted concurrently from all eligible buyers in the following sequence: certified veterans of World War II, Reconstruction Finance Corporation for small business, state and local governments, nonprofit institutions and nonpriority buyers. Orders received after December 10 from both priority and nonpriority buyers will be filled from remaining inventories, WAA said. Federal agencies were previously given an opportunity to fulfil their needs.

VETERANS' BABIES CARED FOR BY THE GOVERNMENT

The Children's Bureau of the Social Security Administration keeps a count of the number of servicemen's babies for whom Uncle Same pays the stork bill, which now amounts to almost $100,000,000. The Emergency Maternity and Infant Care Program, now in its fourth year of operation, is administered by state health departments under plans approved by the U. S. Children's Bureau.

Wives and infants under 1 year of age of men in the four lowest pay grades of the Army, Navy, Coast Guard and Marine Corps are eligible, and care is given even after the servicemen's discharge, if the pregnancy occurred or the infant was under 1 year of age while the husband was in one of the eligible grades. Another hundred thousand babies are on their way, the Children's Bureau reports, and maternity care is being given to their expectant mothers. Besides, more than 180,000 of the babies already born have received or are receiving additional medical, hospital or nursing care during their first year of life.

This care is now costing Uncle Sam about $100 for a maternity case and about $65 for an infant's case. In a few cases with complications the bill runs over $1,000. The amount paid covers the cost of good maternity care, including antepartum care, delivery and care for six weeks after the baby's birth. Doctor, hospital and nurses' bills are all paid, including those for consultation and laboratory services, at rates established under each state plan. Similarly, the medical and hospital bills are paid for the care of a sick baby.

"This wartime emergency measure," Dr. Martha M. Eliot, associate chief of the Children's Bureau, said "turned out to be the largest single public medical care measure for mothers and infants so far undertaken in this country." Besides public health officials and members of their staffs who administered the state program, in one year 48,000 doctors were involved in providing care to these women and their babies. Hospitals everywhere in the country participated. "Many professional workers, motivated by a sense of public obligation, did the job," Dr. Eliot said. "Thanks are due not only the doctors, nurses and hospital staffs but also the countless individuals who took it on themselves to help out in this emergency."

The whole program, it is said, developed out of one person's efforts. Long before Pearl Harbor an army post commander, seeing the plight of many servicemen's families, sought help from the state health department. As a result a request came to the Children's Bureau asking that part of the federal funds available under the Social Security Act for maternal and child health services be used to get care to these servicemen's wives and babies. The request was granted for that state and before a year in twenty-six other states. To meet the emergency in all states, Congress appropriated special funds in March 1943. Certain minimum requirements had to be met by hospitals accepting such cases under the state plans.

CANCER AND THE MEDICAL SCHOOL CURRICULUM

A special committee comprising representatives of fourteen medical schools and of the National Research Council met recently at the National Cancer Institute, Bethesda, Md., with the National Advisory Cancer Council to discuss the place of cancer in the medical school curriculum.

Dr. Frank E. Adair, chairman of the committee, declared that something must be done to improve the education of medical students in cancer, which ranks second as a cause of death in the United States. Among the suggestions made were the establishment of professorships in clinical cancer, greater use of the facilities of cancer diagnosis and cancer prevention clinics, the establishment of cancer institutes or hospitals in connection with medical schools in large urban centers, and greater emphasis in the medical school on the importance of preventive medicine.

A committee to outline a plan of teaching and to make recommendations, which will be sent to all medical schools, will be appointed later.

PERSONAL

The director, Office of Vocational Rehabilitation, Federal Security Agency, has announced the appointment of Dr. Charles L. Newberry as assistant chief medical officer succeeding Dr. Thomas B. McKneely, who was appointed chief medical officer. Dr. Newberry graduated from Marquette Medical School in 1926, engaged in private practice in Milwaukee and was associated with the city health department. On Dec. 7, 1941 he transferred to the Farm Security Administration as senior medical officer and was later commissioned in the U. S. Public Health Service and reassigned to the Farm Security Administration. In January 1945 he joined the United Nations Relief and Rehabilitation Administration as director of health in the Middle East Mission, Cairo, Egypt. Later he went to Vienna as acting chief medical officer to UNRRA in Austria. He returned to the United States in January 1946 and joined the staff of the Office of Vocational Rehabilitation.

MEDICAL OFFICERS RELEASED BY THE NAVY

NAVAL RESERVE MEDICAL OFFICERS RECOMMENDED FOR RELEASE FROM ACTIVE DUTY

Arkansas

Barnett, Horace C.....Heber Springs
Clark, William A.....Little Rock
Taylor, Charles A.....Evening Shade
Woods, Paul H.....N. Little Rock

California

Andersen, George C.....Hermosa Beach
Baker, Edward W.....San Francisco
Bassett, James B.....Orinda
Beland, Arthur J.....Napa
Best, Elbridge J.....San Francisco
Boles, Albert.....Oakland
Bowman, Ralph H.....Corte Madera
Dittes, William L.....Corcoran
Finke, Howard W.....Lynnwood
Gundelfinger, Benjamin F.....Berkeley
Johnston, Ian B.....Berkeley
Lyon, Richards P.....Hidden Valley
Maino, Vernon J.....San Francisco
Martin, James W.....San Francisco
McKenna, John F.....Berkeley
Naman, Marvin J.....Fresno
Quarry, Paul T.....Santa Rosa
Reilly, Eugene V.....San Francisco
Richards, George H.....San Francisco
Smith, Richard C.....San Francisco
Smitter, Robert C.....San Francisco
Steinmetz, John R.....Hayward
Stockton, Andrew B.....San Francisco
Swanson, Marion A.....San Francisco
Sweeney, Alvin R. Jr.....La Jolla
Tufft, Robert W.....San Francisco
Watso, Robert W.....San Jose
Webb, Eugene M.....Berkeley
Wees, Marshall P.....San Francisco
Welke, Elton G.....San Francisco
Wood, David A.....San Francisco
Wrobel, Charles J.....Los Angeles

Florida

McGowan, Thomas R.....Tampa
Morris, Neal.....Pensacola
Zellner, Robert E.....Lakeland

Georgia

Baldwin, Marion A.....Fort Gaines
McClelland, Warren S.....Atlanta
McDuffie, Robert S.....Decatur
Morgan, Horace L.....Savannah
Reeve, Thomas E. Jr.....Calhoun

Idaho

Baum, Mark.....Ashton
Funk, Arthur P.....Boise
Hatch, Charles S.....Idaho Falls

Illinois

Baker, Kenneth C.....Galesburg
Beil, Harry H.....Chicago
Bell, Needham E. Jr.....Bloomington
Domm, Sheldon E.....Naperville
Gregowicz, John J.....E. St. Louis
Ketteman, Charles H.....Chicago
Kionka, Paul F.....Melrose Park
Mann, Raymond J.....Chicago
McLellan, Samuel G.....Evanston
Newman, Melvin M.....Chicago
Roble, Andrew.....Chicago
Samelson, Charles F.....Chicago
Shively, J. Paul.....Chicago
Snow, Garland S.....Dixon
Stein, Irving F. Jr.....Chicago
Stuenner, Harry W.....Chicago
Sutton, George C.....Evanston
Svec, Floyd A.....Chicago
Tierney, James M.....Chicago
Twohey, Joseph T.....Chicago
Wittelle, Frank M.....Chicago
Wolff, Paul G.....Chester
Zvetina, James R.....Chicago

Indiana

Grodrian, Wayne E.....Fort Wayne
Johnson, Robert E.....Muncie
Lambert, C. W.....Indianapolis
Wood, Russell W.....Oakland City

Iowa

Sawin, John F.....Ames
Straub, Joseph J.....Dubuque
Svendsen, Reinert N.....Decorah
Tandy, Roy W.....Morning Sun
Thornton, Thomas F. Jr.....Waterloo
Walsh, William E.....Hawkeye
Westly, John S.....Manly
Young, George G.....Des Moines

Kansas

Freeman, Florian G.....Hutchinson
Hagen, Robert F.....Lawrence
Ratzloff, Dan O.....Kansas City
Stevenson, Charles E.....Parsons
Stone, William F. Jr.....Norton
Wilson, Charles W.....Norton
Wolff, Frederick P. Jr.....Kansas City

Kentucky

Bell, William B.....Hopkinsville
Foster, Richard L.....Louisville
Lewis, Farren C.....Wrigley

Louisiana

Hebert, Warren H.....New Orleans
Smith, Robert C.....New Orleans
Wilkinson, Jacques D.....Alexandria

Maine

Brown, Eugene E.....Bangor
Butterfield, Wilfred I.....Bangor
Leach, Edwin M.....Blue Hill
Webber, Lincoln D.....Kittery

Maryland

Fetter, William J. E.....Baltimore
Futterman, Perry.....Baltimore
Smoot, Merrill C.....Hagerstown

Massachusetts

Brenner, Louis.....Dorchester
Brown, Robert H.....Hyde Park
Casterline, Donald G.....Malden
Clancy, Daniel H. Jr.....Weymouth
Cranley, John J. Jr.....Medford
Cruickshank, Frank S.....Boston
Curran, John F. Jr.....Worcester
Elliott, Frederick D.....Boston
Foote, John J.....Dorchester
Freedman, Lawrence Z.....Worcester
Goehring, H. D.....Newton Upper Falls
Hopkins, Lawrence T...Wellesley Hills
Kenny, Donald E.....Medford
Kunin, Kalman C.....New Bedford
Leach, Russell E.....Lowell
Maiella, Anthony M.....Brookline
Mansfield, Thomas R.....Framingham
Marco, Philip J.....Boston
Marsh, Carl G.....Worcester
Patchett, Orval W.....Amesbury
Peterson, Norvell L.....Boston
Petetsman, Jacob.....Somerville
Robinson, James W.....Auburndale
Sennott, Francis W.....Cambridge
Smith, Leonard K.....Springfield
Stone, Jacob M.....Brookline
Sweeney, John D.....Waltham
Tsolas, George J.....Watertown
Wales, Burton L. Jr.....Abington
Warren, Shields.....Boston
Warthen, Robert O.....Kensington
Watson, Wilfred M.....Northboro
Weiss, Jess B.....Brookline
Welch, Kenneth J.....Waban
Zanca, Ralph.....Marlboro

Minnesota

Eisenman, Walter.....Chisholm
Flom, Reynold P.....Minneapolis
Karlson, Karl E.....St. Paul
Lewis, Charles W.....Minneapolis
Marshall, Clark M.....Minneapolis
Martin, Frank E.....Minneapolis
Schoeberl, Cletus B.....Slayton
Walker, Philip H.....Wayzata
Westover, Darrell E.....Richville
Wilder, Russell M. Jr.....Rochester

Mississippi

Magee, Louis M.....Natchez
Miller, Archie C.....Hazlehurst
Von Hasseln, Edmund W...Brooksville

Missouri

Juden, Alexander G.....Cape Girardeau
Kraft, Jacob.....Kansas City
Meritt, Joseph E. Jr.....Rhineland
Willmott, Robert O.....St. Louis

Nebraska

Kleager, Clyde L.....Alda
Pester, George H.....Broken Bow
Protzman, Frank W.....Omaha
Weare, Clifford S.....Stamford
Wilcox, Malcolm B.....Kearney
Wisner, Harry J. Jr.....Scottsbluff

New Hampshire

Baker, Sidney R.....Rochester
Dignam, William J.....Nashua
French, Rowland B.....Hanover
Sewell, Elmer M.....Greenland
Smith, Thomas J. Jr.....Dover
Sterling, Franklin W.....Hillsboro
Thibault, Hector H.....Greenville

New Jersey

Case, Clarence E. Jr.....Somerville
Harris, Carl A.....Cedar Grove
Hoffmann, George T.....Orange
Jackson, Francis C.....Rutherford
Murphy, Ian D.....Ventnor City
Troast, Leonard.....Nutley
Padovano, Joseph.....Boonton
Van Mater, John S.....Highland Park
Weisbrod, Lawrence M.....Newark

New York

Ballew, James R.....New York
Belden, Daniel C.....New York
Berg, Irving D.....New York
Brezing, Robert P.....New Rochelle
Brockmyer, Merlin L.....Rochester
Brown, Philip.....New York
Buholtz, Wilbur S.....Churchville
Cavallarom, Salvatore E.....Jamaica
Chessid, Sigmund E.....Brooklyn
Clarke, Francis E.....Valley Stream
Davis, John E.....Troy
Dichter, Lionel.....Bronx
DuBilier, Benjamin.....Staten Island
Dworsky, Alexander.....Brooklyn
Dyke, Joseph S.....New York
Fagan, James H. Jr.....New York
Farley, William J.....Flushing
Fisher, Lyman R.....Waverly
Fountain, Gerald Jr.....Scarsdale
Frank, Nathan R.....Brooklyn
Fraser, William E.....Scarsdale
Gall, Henry.....Bronx
Genninger, Lewis E.....Bellerose
Gitlin, Louis F.....Jamaica
Goldberg, Robert S.....Bronx
Gottlieb, Mack L.....New York
Gorman, Gerald P.....Staten Island
Grosberg, Saul J.....New York
Guyer, Donald C.....Albany

MEDICAL OFFICERS RELEASED BY THE NAVY

New York—Continued

Hale, Harry W. Jr.....Stillwater
Harrison, Harlon W.....Albany
Henneman, Elwood.....Pelham
Hoch, Peter C.....Verona
Hoge, Leo J. Jr.....Saratoga Springs
Houston, Charles S.....Great Neck
Howard, Samuel W.....St. Albans
Iaia, Bartolomeo D.....Auburn
Ippolito, Carlo A.....Bronx
Jenkins, Harry A.....Rockville Center
Johantgen, Henry F.....Rochester
Kayden, Herbert J.....New York
Kertzner, Bertram.....Brooklyn
Klatzko, Morris.....Brooklyn
Kleinman, Herman.....Brooklyn
Knott, Nairn D.....Albany
Knox, William G. Jr.....Manhasset
Koloski, Eugene L.....Port Richmond
Krech, Sheppard Jr.....New York
LaVerdi, Charles Jr.....Bronx
Levitt, Earl.....New York
Lohnaas, Harold.....Brooklyn
McCutcheon, James G.....Marilla
Meltzer, Saul B.....Elmira
Milhauser, Jack W.....Brooklyn
Miller, Otis B.....Cedarhurst
Mott, Howard O.....Schenectady
Moyer, Jason K. Jr.....Binghamton
Noshay, William C.....Eggertsville
Pietraszek, Casimir F.....Buffalo
Radzimski, Eugene H.....Buffalo
Ross, Bernard.....Brooklyn
Ruskin, Richard A.....New Rochelle
Sayer, Arthur.....New York
Scal, Howard.....New York
Scherl, Siegfried.....Bronx
Smith, Alfred H. Jr.....Richmond Hill
Soiefer, Jack.....Brooklyn
Stubenbord, John G. III....Douglaston
Thompson, Alden S.....New York
Thomson, Archibald W. Jr....New York
Toothaker, Bernard L.....New Rochelle
Tortora, Anthony R.....Brooklyn
Trutletaub, Gerald N.....Brooklyn
Tumarkin, Bernard.....New York
Turbin, Joseph.....Brooklyn
Von Glahn, Harold D.....Brooklyn
Walker, Donald C.....Delanson
Walsh, John W.....Bellerose
Walsh, Robert E.....Elmira
Warner, Nathaniel.....New York
Weissman, Morris P.....Bronx
Wilbur, Harry J.....Walton
Wilson, James R.....Utica
Wisengrad, Michael.....Belle Harbor
Wood, Edward F.....Rochester
Wren, Robert S.....Ossining
Young, Willis W.....Watertown

North Carolina

Camblos, Joshua F.....Asheville
Hall, John M.....Elkin
Holden, William B.....Wake Forest
Lewis, Clifford W.....Beaufort
Lyda, Edgar W.....Winston-Salem
Trachtenberg, William...Winston-Salem
Watson, Wm. Mobley.....Asheville

North Dakota

Dahlen, Gregory A. Jr.....Bismarck
Perkins, Neal C.....Grand Forks

Ohio

Bova, George S.....Toledo
Boyd, Foster J. Jr.....Cincinnati
Fening, Walter E.....Hamilton
Hamilton, Frederick G.....Cleveland
Maggied, Sol.....Columbus
Manchester, Robert C.....Alliance
Sonnemann, Charles C.....Cincinnati
Wiseman, George R. Jr.....Amherst
Wulsin, John H.....Cincinnati
Zeligs, Meyer A.....Cincinnati

Oregon

Achterman, Walter H.....Eugene
Barclay, Charles G.....Portland
Cochran, Quinten W.....Portland
Goddard, Edward P.....Klamath Falls
Hall, Richard E.....Portland
Havard, Clarence E.....Grants Pass
Kavanaugh, John D.....Portland
Livingston, William K.....Portland
Loomis, John W.....Portland
McMurray, William R. Jr.....Portland
Mason, David C.....Beaverton
Meek, Edward C. Jr.....Portland
Patton, Robert W.....Portland
Spence, Harry Y.....Eugene
Toon, Robert W.....Aurora

Pennsylvania

Boughton, Robert M.....Erie
Brickhouse, Herman M.....Warren
Brown, Henry.....Erie
Burkle, Joseph S.....Philadelphia
Calesnick, Benjamin.....Philadelphia
Cooper, Albert F.....Wilkes-Barre
Corneal, Forrest B.....Philadelphia
Cressman, Paul G. Jr.....Lewistown
Doane, John H. Jr.....Mansfield
Eckenrode, Joseph L.....Lancaster
Erickson, Elmer W.....Irwin
Fargotstein, Ralph.....Pittsburgh
Faris, Samuel S. II.....Glenside
Franke, Frederick R.....Pittsburgh
Garey, James L.....State College
Gerber, Paul.....Philadelphia
Gilchrest, James W.....Derry
Hallahan, John D.....Lansdowne
Harrison, Joseph Jr.....Villanova
Holland, Robert H.....Red Lion
Johnson, Thomas B.....Towanda
Kane, James A. .....Dunmore
Knerr, Edgar D. Jr.....Coopersburg
LeFever, Robert S.....Gettysburg
Lehan, Thomas R.....Erie
Lichtenstein, Irving L.....Philadelphia
Lotz, Glenn W.....McKeesport
McBurney, James W.....Rochester
McCune, Wallace G.....Ellsworth
Meli, John J.....Charleroi
Nealon, Thomas F. Jr.....Jessup
Pelosi, Louis M.....Philadelphia
Politano, Victor A.....Point Marion
Scarpitti, William F.....Philadelphia
Schaefer, Robert L. Jr.....Jeannette
Schaeffer, William A.....Lancaster
Shiring, Francis J.....Pittsburgh
Stauffer, Herbert M.....Philadelphia
Sterner, Robert F.....Cheltenham
Williams, Bryan V.....Pittsburgh
Williamson, Neihl J.....Jersey Shore
Wilson, Joseph W.....Pittsburgh

Rhode Island

Bliss, Joseph A.....Woonsocket
Chapman, James G.....Pawtucket
Curran, Edmund B.....Edgewood
Lomasney, Thomas L.....Pawtucket
Lynam, Patrick J.....Jamestown
Murphy, William F.....Newport
Sonkin, Nathan.....Pawtucket
Stoops, William A.....Newport

South Carolina

La Borde, Oscar.....Columbia
Pringle, Robert A.....Charleston
Skinner, Charles B.....Hartsville
Thomas, Ben D.....York
Whitesides, William C. Jr.....York
Workman, John A.....Woodruff

South Dakota

De Richards, Paul.....Sturgis
Feeney, Michael J.....Pierre
Perman, Harvey H.....Eureka
Stern, Charles A.....Sioux Falls
Thorpe, Virgil L.....Hudson
Vincent, John W.....Rapid City

Texas

Atkinson, George N.....Shamrock
Bailey, Joe W.....Austin
Buie, Neil D. Jr.....Marlin
Cameron, Bruce M.....El Paso
Daily, Louis Jr.....Houston
Gaddy, Howell R. Jr.....Lampasas
Gordon, William H. Jr.....San Antonio
Heiligman, Emmett M.....Overton
Lehmberg, Seth W.....Georgetown
Leifeste, Homer F.....Madisonville
Liles, Ralph.....Houston
Mathis, Robert L.....San Antonio
Payne, Beverly C. Jr.....Beaumont
Rainer, James W.....Austin
Roach, Paul A.....Ladonia
Smith, Lex B.....Teague
Spencer, James R. Jr.....Galveston
Ward, James F.....Lubbock
Williams, Frank C. Jr.....Los Fresnos
Woodward, Joe W.....Sweetwater
Worley, Gordon Jr.....Austin

Utah

Adams, Richard P.....Manti
Barton, Ray H. Jr.....Salt Lake City
Dalton, Willis V.....Salt Lake City
Hughes, Grant B.....Salt Lake City
Johnson, Gordon S.....Salt Lake City
McMurrin, James A.....Logan
Merrill, Laville H.....Standardville
Sharp, Max W.....Lehi
Spencer, LeGrand D.....Logan
Sweeney, Michael J.....Salt Lake City
West, Charles D.....Ogden
Woolsey, Carl T.....Salt Lake City

Vermont

Agan, Robert W.....Bennington
Brown, Clarence H.....Rutland
Keenan, Edward A.....Burlington
Shorey, Winston K.....Lyndonville

Virginia

Craddock, Charles G. Jr.....Lynchburg
Stuart, Royal E.....Charlottesville
Terry, William S.....Gretna
Waters, Louis N.....Portsmouth

Washington

Goss, Clark C.....Seattle
Lauer, Paul R.....Seattle
Snyder, Richard V.....Seattle
Swinehart, Loy T.....Spokane

West Virginia

Aliff, Robert C.....Huntington
Bailey, Robert F.....Craigsville
Berry, Robert Z.....Flatwoods
Brown, Donald P.....Kingwood
Carlson, Frederick B.....Charleston
Carter, Warren S.....Huntington
Curry, George A.....White Sulphur Spr.
Edmiston, John M.....Buckhannon
Eckley, George M. Jr.....Beckley
Fankhauser, Robert K.....Parkersburg
Hogshead, George W.....Montgomery
Holswade, George R.....Spencer
Leonard, James B.....Parkersburg
Scott, Charles N.....Smithfield
Seabright, Howard L.....Wheeling
Vest, James C.....Whitesville
Wiser, Henry J.....Bluefield

Wisconsin

Chrest, Clarence P.....Madison
Coffey, William L. Jr.....Wauwatosa
Florin, Alvin C.....Fond du Lac
Lukes, Richard E.....Milwaukee
Millen, Francis J.....Milwaukee

Wyoming

Cranney, Wyndon D.....Auburn
Knebel, John A.....Buffalo
Sullivan, Bernard J.....Laramie

Medical News

(PHYSICIANS WILL CONFER A FAVOR BY SENDING FOR THIS DEPARTMENT ITEMS OF NEWS OF MORE OR LESS GENERAL INTEREST: SUCH AS RELATE TO SOCIETY ACTIVITIES, NEW HOSPITALS, EDUCATION AND PUBLIC HEALTH.)

ALABAMA

University News.—The Medical College of Alabama, Birmingham, announces the receipt of two grants made to Joseph K. Cline, Ph.D., associate professor of biochemistry. Distillation Products, Inc., awarded $2,500 for research in vitamin E therapy, and a grant of $7,500 by the Research Corporation for a study of antianemic substances was made this month. In studying the antianemic substances he will work with substances that stimulate the regeneration of red blood cells and will attempt to determine the mechanism of their actions. Dr. Cline, formerly director of the laboratory of the nutrition clinic at the Hillman Hospital, was appointed to the faculty of the medical college in March. Dr. Joseph F. A. McManus has been appointed assistant professor of pathology at the Medical College of Alabama. Dr. McManus served in the Royal Canadian Army Medical Corps from September 1940 to 1945; he joined the Medical College of Alabama after doing research in histochemistry at the University Museum, Oxford, England. Clarence E. Klapper, Ph.D., and his wife, Margaret Strange Klapper, have been appointed assistant professor in anatomy and instructor in the department of medicine, respectively.

CALIFORNIA

Personal.—Dr. Willis L. Jacobus Jr. has been appointed athletic medical director of the University of Southern California, Los Angeles. He succeeds Dr. Packard Thurber Jr., who resigned after holding the position for twenty-one years to devote all his time to general practice.

Position Available.—The Los Angeles Psychiatric Service, an adult community mental hygiene clinic supported by the Community Chest, has an opening for a psychiatrist-director to give full time to the clinic. The requirements are that the director be a specialist certified in psychiatry and have some administrative experience. The clinic personnel includes volunteer psychiatrists, two psychiatric social workers and a psychologist. The salary is in accordance with qualifications. Address the Los Angeles Psychiatric Service, 507 South Westlake Avenue, Los Angeles 5.

CONNECTICUT

New Medical Director of Welfare Department.—Dr. Philip W. Fenney of West Haven has been appointed medical director of the Connecticut State Welfare Department. The appointment of Dr. Fenney, a veteran of World War II, is on a temporary basis with examination for the position to be held later, according to the statement of Commissioner Robert H. Smith. Dr. Fenney succeeds Dr. Leonard Parente, who resigned last month after four years with the department, to become health officer of Hamden.

Centenpial Meeting of Hartford Medical Society.—As part of the observance of the one hundredth anniversary of its founding in 1846, contemporary members of the society reenacted an early meeting of the Hartford County Medical Society on September 16 at the Hunt Memorial Building, 38 Prospect Street, Hartford. The program closed with a dinner meeting and address by President G. Keith Funston of Trinity College on "Liberal Education and Its Relation to Medicine." Each member present received a copy of the historical volume published for the occasion and entitled "The First Century of the Hartford Medical Society."

Liaison Committee on Occupational Health.—The governing council of the Connecticut State Medical Society has appointed a liaison committee to the new Institute of Occupational Medicine and Hygiene at Yale University, New Haven. Members of the new committee are Dr. Thomas P. Murdock, Meriden, council chairman; Dr. Creighton Barker, New Haven, executive secretary, and Dr. Charles F. Yeager, Bridgeport, chairman of the society's committee on industrial health. The institute will be headed by Dr. Ronald F. Buchan, West Hartford, recently appointed assistant professor of industrial medicine, who will serve as the clinical director (THE JOURNAL, November 9, p. 591).

GEORGIA

Joint Meeting.—Dr. Frank H. Lahey, Boston, was among the speakers October 1 at a meeting which was the first annual session of the Georgia chapter of the American College of Surgeons and the fall meeting of the Fifth District Medical Society. The session, held in Atlanta, also included clinics. Dr. Lahey discussed "The Management of Lesions of the Stomach, Duodenum and Jejunum."

ILLINOIS

Personal.—The town of Kempton held a community dinner in the local high school November 3 to honor Dr. William G. Ross on his seventy-seventh birthday. Dr. Ross, who has practiced in Kempton for forty-three years, was presented with a radio.

Chicago

Walter Theobald Heads Medical Center Commission.—Dr. Walter H. Theobald on November 20 became chairman of the Medical Center Commission, succeeding Dr. Raymond B. Allen, who resigned to become president of the University of Washington.

Lecture by British Biochemist.—Dr. Douglas Robertson, professor of biochemistry, Middlesex Hospital Medical School, London, lectured at the University of Illinois College of Medicine November 8 on "The Nature of the Disturbed Calcium and Phosphorus Excretion in Thyrotoxicosis and Myxedema."

Charles Swift Retires.—Dr. Charles H. Swift, associate professor and secretary of the department of anatomy at the University of Chicago School of Medicine, has been retired with emeritus status, it was announced November 26. Dr. Swift, who has reached the university's automatic retirement age, has been associated with the university for the past forty-seven years; he graduated at Rush Medical College in 1910.

The Ranson Lecture.—Dr. Albert M. Snell, chief of the section on medicine, Mayo Clinic, Rochester, Minn., and professor of medicine in the Mayo Foundation, delivered the annual Stephen Walter Ranson Lecture, sponsored by the Phi Beta Pi Fraternity, at Northwestern University Medical School on Tuesday, December 3. The lecture was presented at Thorne Hall, on the Chicago campus of Northwestern University, at 5 p. m. Dr. Snell's subject was "Recent Advances in the Field of Hepatic and Biliary Disease."

Herman Smith Resigns at Michael Reese.—Dr. Herman Smith has resigned as executive director of Michael Reese Hospital to become a hospital consultant on a full time basis in Chicago. He leaves Michael Reese after twenty-six years' service. Dr. Morris H. Kreeger, assistant director of Mount Sinai Hospital, New York City, from 1940 to 1946, arrived at Michael Reese November 18 to take over the executive directorship of the hospital. Dr. Kreeger graduated at Jefferson Medical College in Philadelphia in 1935 with prizes in surgery, neurology and ophthalmology and was in general practice in Bloomfield, N. J., from 1937 to 1939.

INDIANA

Students Win Awards.—The Osterman awards of the Indiana University School of Medicine, Indianapolis, have been announced as follows:

First prize, $20, John Edward Ross, Experimental Hemothorax.
$15 prizes: Don G. Buck, Lesions of the Spinal Epidural Space Producing Cord Compression.
Charles E. Buck, The Bleeding Nipple.
Gilbert B. Causey, Early Diagnosis and Management of Small Intestinal Obstruction.
Charles C. Gullet, Vagotomy for Gastroduodenal Ulcer.
Paul William Holtzman, Regional Enteritis.
John W. Mason, Jaundice, Surgical Considerations.
Roy V. Maxson, Traumatic Rupture of the Spleen.
$10 prizes: Davis A. Baltz, Congenital Cystic Lung. Pneumonectomy in a 3 Week Old Baby.
Robert P. Buckler, The Immersion Foot Syndrome.
Robert D. Cunningham, Causalgic States in Peace and War.
John H. Grant, Studies in Experimental Vascular Surgery.
George T. Lukemeyer, Shock and Refrigeration.
$5 prizes: John W. Geddes, Management of Abdominal Wounds in Warfare.
Oscar Green, Thrombophlebitis, Experience at an Army General Hospital.
August M. Kasper Jr., Refrigeration Anesthesia.
Theodore R. LeMaster, A Review of Posttraumatic Renal Injury.
John R. Porter, A Study of Shock in Battle Casualties.

The Osterman Prizes were established by Mr. H. Osterman, Seymour, in 1939 for outstanding papers by students in the medical school (THE JOURNAL, Nov. 25, 1939, p. 2011). The recipients are chosen by the editorial board of the *Quarterly Bulletin*, published by the medical school.

MARYLAND

New Radiology Department at Johns Hopkins.—Dr. Russell H. Morgan, former associate professor of radiology at the University of Chicago, has been made professor of radiology in the Johns Hopkins University School of Medicine and radiologist in chief at the Johns Hopkins Hospital, effective about January 1. Dr. Morgan will be in charge of a new department of radiology created at the university and the hospital. Radiology, formerly a section in the division of surgery, has been made an independent department of the two Hopkins institutions in order to provide better clinical service at the hospital, to improve instruction in the university and to promote research in this increasingly important field.

MASSACHUSETTS

Personal.—Dr. Abraham Cohen, Philadelphia, and Dr. Loring T. Swaim, Boston, were guest speakers at the recent convention of the International Society of Medical Hydrology at Buxton, England, on "Treatment of Arthritis."——Dr. Henry D. Chadwick, Cambridge, state health commissioner of Massachusetts from 1933 to 1938, retired recently as medical director and superintendent of the Cambridge Sanatorium, a position he had held since 1942.——Albert H. Hegnauer, Ph.D., Syracuse, N. Y., and Dwight J. Mulford, Ph.D., Boston, have been appointed associate professor of physiology and assistant professor of pharmacology, respectively, at Boston University School of Medicine.

MISSOURI

Personal.—On September 4 Andrew H. Panetiere Post number 490 honored Dr. Edwin C. White, Kansas City, particularly in gratitude for the news letter which he edited and which was sent to the members of the Jackson County Medical Society, including those who were in service.

Faculty Changes.—Recent faculty changes in the St. Louis University School of Medicine include the following: Dr. Percy J. Carroll (brigadier general, U. S. Army, retired), assistant dean and professor of public health; Dr. Mark C. Wheelock, assistant professor of pathology, and Dr. Paul A. Murphy, assistant professor of pharmacology.

Lawyer Appointed to Health Post.—On August 31 Samuel Marsh, a lawyer of Kansas City, was named by Governor Donnelly as director of public health and welfare. The appointment is subject to confirmation by the senate. As director of the department of public health and welfare Mr. Marsh is administrative head of three divisions, public health, mental diseases and welfare. According to the Kansas City *Star* his office will manage the state hospitals and the social security program in Missouri.

NEW YORK

Cancer Teaching Day.—On December 12 a Cancer Teaching Day will be presented in Troy under the auspices of the Medical Society of the County of Rensselaer, Tumor Clinic Association of the State of New York, the state medical society and the New York State Department of Health Division of Cancer Control. The speakers will include:

Dr. Hayes Martin, New York City, Mouth Cancer.
Dr. Cushman D. Haagensen, New York City, Tumors of the Breast.
Dr. Louis C. Kress, Buffalo, Tumors of the Bone.
Dr. Richard B. Cattell, Boston, Malignant Tumors.
Dr. Harold W. Dargeon, New York City, Tumors in Children.

New York City

The Brickner Lecture.—The Hospital for Joint Diseases announces that the 1946 Walter M. Brickner Lecture will be delivered by Dr. Arnold R. Rich, professor of pathology at the Johns Hopkins University School of Medicine, Baltimore, December 12, at the hospital. The subject is "Problems Relating to the Pathogenesis of Cirrhosis of the Liver."

Consulting Pneumatologist Named for Hospital.—Dr. Paluel J. Flagg was appointed consulting pneumatologist to the Manhattan Eye, Ear and Throat Hospital November 21. The action was taken by the board of directors of the hospital at the recommendation of the board of surgical directors. The action was said to stem from a resolution passed by the House of Delegates of the American Medical Association, December 4, 1945.

Julius Jarcho Honored.—Dr. Julius Jarcho was guest of honor at a dinner November 21 to mark his retirement as president of the medical board of Sydenham Hospital. A feature of the occasion was the dedication of the library of the hospital to him and named the Dr. Julius Jarcho Library. Dr. Jarcho has been associated with Sydenham Hospital for the past forty years and served as president of the medical board during the latter ten years. He is attending surgeon in obstetrics and gynecology at Sydenham and is the author of several textbooks and treatises on obstetrics and gynecology which are used in medical teaching. Dr. Jarcho graduated at Columbia University College of Physicians and Surgeons in 1904.

Erythroblastosis Fetalis Clinic.—The Jewish Memorial Hospital has established a clinic for the study and treatment of erythroblastosis fetalis under the direction of Dr. Harry Wallerstein, hematologist to the hospital, in collaboration with Drs. Milton J. Goodfriend, attending obstetrician, Michael Schuman, attending pediatrician, Alfred Angrist, director of laboratories, and Philip Levine, consulting serologist. The clinic solicits specimens for study from cases presenting implications of erythroblastosis fetalis. In suitable cases mothers will be accepted for admission to the antepartum clinic and/or delivery. Babies born outside this institution in whom the suspicion of erythroblastosis exists will also be accepted for admission. Further information will be obtained from the superintendent of the Jewish Memorial Hospital.

Portrait of Dr. Rowland G. Freeman.—On November 20 a portrait was unveiled of Dr. Rowland G. Freeman at the New York University College of Medicine. The portrait, a gift to the college by Dr. Rowland G. Freeman, son of the late Dr. Freeman, was painted by the artist William J. Whittemore, an intimate friend of the late Dr. Freeman. Dr. Freeman developed methods of studying the bacteria in milk. He with other members of the college faculty organized a milk commission supervising certified milk production in New York City. Dr. Freeman was the first secretary of the commission. He was also chairman at the time of his death on Nov. 14, 1945, a position he held for twenty-eight years. Dr. Freeman graduated at Columbia University College of Physicians and Surgeons. He joined the New York University faculty in 1898 as chief of the pediatric clinic. He was made professor of pediatrics in 1920, becoming emeritus with his retirement in 1930.

Grant-in-Aid for Tropical Medicine.—The department of preventive medicine, New York University College of Medicine, has received a grant-in-aid from the American Foundation for Tropical Medicine to assist in establishing a unit for the development of tropical medicine and parasitology in connection with Bellevue Hospital. The unit will consist of a clinician, Dr. Harry Most, a parasitologist, Donald V. Moore, Ph.D., and a technician. A diagnostic laboratory will be set up in connection with the third (New York University) division of Bellevue Hospital for the examination of blood and fecal specimens. The laboratory will also serve other divisions of the hospital as examinations are requested. It will also furnish teaching material for medical students. Dr. Most and Dr. Moore will act as consultants to the clinical staff and will conduct the teaching program in tropical medicine and parasitic diseases in the medical school. Dr. Most has been on leave of absence for service in the army. He has been in charge of the tropical medicine section of Moore General Hospital, Swannanoa, N. C. Dr. Moore comes to the department from the State Health Department of Texas, where he has been in charge of the parasitology division of the state laboratory.

NORTH CAROLINA

Medical Lectures.—The Matheson Foundation Medical Lectures, sponsored by the Matheson Foundation and the Mecklenburg County Medical Society, was held in Charlotte at the Hotel Charlotte, October 31-November 1. Among the speakers were:

Dr. Henry L. Bockus, Philadelphia, Clinical Aspects of Infectious Hepatitis.
Dr. Donald G. Anderson, Boston, The Treatment of Infections with Penicillin and Streptomycin.
Dr. Isidor S. Ravdin, Philadelphia, Some Problems in Biliary Tract Surgery.
Dr. Edward A. Schumann, Philadelphia, Obstetric Hemorrhage.
Drs. Cyrus C. Sturgis and Carl V. Weller, Ann Arbor, Clinicopathologic Conference.
Dr. Francis E. McDonough, Boston, The Diagnosis and Medical Management of Lesions of the Stomach, Duodenum and Jejunum.
Dr. Frank H. Lahey, Boston, The Surgical Management of Lesions of the Stomach, Duodenum and Jejunum.

OHIO

Research on Coronary Occlusion.—Under two grants totaling $7,000 from the U. S. Public Health Service Dr. Roy W. Scott, professor of clinical medicine, Western Reserve University School of Medicine, and his associates at University and City hospitals in Cleveland, will administer carefully controlled doses of Dicumarol (3-3'-methylene-bis-[hydroxycoumarin]) to men and women hospitalized after attacks of coronary occlusion. In announcing the project Dr. Scott said

he was encouraged to carry on the work as a result of a few reports in the medical literature indicating that Dicumarol may appreciably lower the death rate from heart disease by preventing the clots from blocking the circulation in other parts of the body. As president of the American Heart Association last year Dr. Scott appointed a committee to direct a cooperative study of Dicumarol by several institutions. For this study the U. S. Public Health Service has contributed a total of $35,000. At University Hospitals the program is being conducted by Dr. Joseph M. Hayman Jr., professor of clinical medicine and therapeutics at Western Reserve, and Dr. Harold Feil, associate clinical professor of medicine.

OKLAHOMA

Changes in Health Officers.—Included among recent appointments to the Oklahoma State Department of Health are those of Drs. George W. Winn, Lawton, county superintendent of health of Comanche County; James M. Gordon, Ardmore, county superintendent of health of Carter County; William W. Cotton, Atoka, county superintendent of health of Atoka County, and Alfred R. Sugg, Ada, county superintendent of health of Pontotoc County.

PENNSYLVANIA

Philadelphia

Personal.—Dr. Abraham Cohen was recently a guest speaker at the convention of the International Society of Medical Hydrology in Buxton, England, on the "Treatment of Arthritis."——Dr. William P. Bager Jr., medical director and internist, St. Luke's Hospital, Bluefield, W. Va., has been appointed associate medical director of Sharp and Dohme.

Penicillin or Silver Nitrate in Ophthalmia Neonatorum.—On November 7 a resolution was presented to the Eye Section of the Philadelphia County Medical Society requesting the appointment of three members, one an ophthalmologist, one a gynecologist and one a bacteriologist, to constitute a committee known as the Committee on the Prevention of Ophthalmia Neonatorum. The resolution urged that this committee undertake a study with the view of determining whether silver nitrate may be abandoned altogether and whether penicillin would be more effective in the treatment of the expectant mother and as a preventive agent in the eyes of the newborn. The resolution points out that the action should be taken because penicillin is universally recognized as a bacteriostatic agent possessing chemotherapeutic properties against the gonococcus and other organisms; silver nitrate has been used since 1884 as a chemical to prevent ophthalmia neonatorum caused by the gonococcus and other organisms; ophthalmia neonatorum has not been completely eliminated despite the use of silver nitrate; silver nitrate in 1 and 2 per cent solutions may cause a chemical conjunctivitis; the prevention of ophthalmia neonatorum is concerned primarily with the prevention of gonorrhea in the expectant mother, and gonorrhea may be treated and cured in the expectant mother with the use of penicillin.

Pittsburgh

The Huggins Memorial Lecture.—On November 22 Dr. Paul R. Cannon, chairman, department of pathology, University of Chicago School of Medicine, lectured on "Clinical Approach to the Problem of Protein Deficiency Disease." The lecture was given at the University of Pittsburgh School of Medicine under the auspices of chapter Nu of the Phi Delta Epsilon Fraternity.

VERMONT

State Health Council Created.—On November 15 the Vermont state health council was organized to coordinate health programs in the state. Representatives of twenty-nine Vermont organizations participated in the initial meeting. The meeting was sponsored by the Vermont State Medical Society. The constitution of the new council embodies many of the principles of the governor's twenty-two point health program. According to the Rutland *Herald*, November 16, the object of the new group is revision and expansion of the state public health department, "integration" of public health department and college of medicine laboratories, establishment of small rural health centers, expansion of nutrition programs, control and eradication of tuberculosis, venereal diseases, undulant fever and other communicable diseases, also diagnosis, care and treatment for other diseases and increased maternal health services, child health service expansion to include medical and dental examinations and immunization, and extension of treatment and care of the mentally ill and mentally deficient. Other programs outlined included support of the college of medicine at the University of Vermont, promotion of hospital development, efforts to make the practice of medicine in rural areas more attractive, correct pay inequalities for health and hospital personnel, promotion of the education, training and welfare of the nursing and the pharmaceutical professions and the supporting of legislation to the ends outlined. Dr. Frank C. Angell, Randolph, president of the Vermont State Medical society, was elected chairman. Other officers include Howard Reid, D.D.S., Vermont State Dental association, vice chairman, Mr. John W. Brownlee, executive secretary, Vermont State Medical society, secretary, and Stanley G. Judd, commissioner of agriculture, treasurer.

WEST VIRGINIA

Approved New Cancer Center.—At a meeting of the executive committee of the West Virginia Cancer Society, Inc., October 31, at Clarksburg Mr. Homer Gebhart of Huntington, treasurer of the society, was named disbursing agent for all county and local cancer organizations. The establishment of a cancer information center, with a cancer field worker recommended by the project committee, was unanimously approved. The committee directed that, of the 60 per cent of funds realized from cancer drives which will remain in this state, 15 per cent is to be utilized for administrative expenses at the state offices. The remaining 45 per cent may be expended as follows: An approved project in any county may spend up to 45 per cent of that county's annual contribution. If the full 45 per cent is not sufficient to finance the approved project, the executive committee can appropriate from the state general fund a sufficient amount to take care of the balance, and an adjoining or adjacent county to an approved project may allocate its entire 45 per cent to that project. The preliminary report of the project committee, submitted by Dr. Paul R. Gerhardt, chairman, and Drs. Thomas L. Harris and Richard O. Rogers and approved by the executive committee, provides that all local projects must have the approval of the cancer committee of the local medical society. The committee unanimously disapproved the affiliation of county cancer organizations with community chest drives.

Hospital Survey.—The sum of $22,500 has been allocated by Governor Clarence W. Meadows from his emergency fund to cover the state share of the cost of a statewide hospital survey, which will be made under the provisions of the recently enacted Hill-Burton bill whereby Congress appropriated $75,000,000 a year for five years for the construction of hospitals, medical centers and clinics throughout the country. West Virginia's share is $1,555,000 per year. This state will receive $11,250 from the federal government to help finance the survey which is required under the provision of the bill. The survey will be under the immediate supervision of Dr. Newman H. Dyer, state health commissioner. Dr. Paul R. Gerhardt, director of the division of cancer control, will serve as consultant and medical adviser. Much of the preliminary work has already been completed by Mrs. George Fordham, a member of the state health department's administrative staff. It is expected that the budget, which was prepared and mailed to Washington early in November, will be approved without delay, and it is hoped that the survey may be completed within the next four to five months. An advisory committee is to be appointed by the governor which must approve any report that is submitted to Washington for consideration by the U. S. Public Health Service. The bill provides for the construction of hospitals, clinics and medical centers by states, counties, municipalities and nonprofit organizations.

WISCONSIN

Helmholz Lecture.—Sir Lionel E. H. Whitby, C.V.O., M.C., M.A., M.D. Cantab., F.R.C.P. Lond., D.P.H., currently regius professor of physic, department of medicine, University of Cambridge, and honorary consulting hematologist to the Royal Army Medical Corps, delivered the A. C. Helmholz Lecture before the faculty and students at the school of medicine, University of Wisconsin, November 19. The subject of the lecture was "Hematologic Effects of Radiation."

Annual Preceptors Meeting.—On November 22-23 the University of Wisconsin Medical School resumed its annual scientific meeting for the associated teaching staff of preceptors. The preceptorial staff consists of physicians in various localities throughout the state and carries out a part of the extramural teaching of senior medical students. Each fourth year medical student spends twelve weeks with one of the preceptorial groups. This is made possible by making the fourth year of the medical course twelve months in length rather than nine months. The program was arranged by the faculty of medicine in Madison

and took place in the auditorium of the Service Memorial Institute building of the medical school and in the wards of the State of Wisconsin General Hospital. The program included:

Paul F. Clark, Ph.D., Oswald S. Orth, Ph.D., and Dr. Ovid O. Meyer, Symposium on the Antibiotics.
Dr. Sture A. M. Johnson, Cutaneous Manifestations of Some Common Medical Conditions.
Dr. Edgar S. Gordon, The Management of Some Difficult Metabolic Problems.
Dr. Daniel Murray Angevine, Fatal Pulmonary Embolism.
Dr. William D. Stovall, Hemolytic Reactions, Transfusions and Erythroblastosis.
Dr. Warren E. Gilson, Electronics in Research and Clinical Medicine.
Drs. Helen A. Dickie and Joseph W. Gale, Current Medical and Surgical Aspects of Tuberculosis.
Dr. William S. Middleton, Some Medical Aspects of World War II.

GENERAL

Congress on Obstetrics and Gynecology.—The American Congress on Obstetrics and Gynecology will be held in the Municipal Auditorium in St. Louis, Sept. 8-12, 1947. The second congress was held in the same place in 1942 and the first congress in Cleveland in 1939. Dr. Fred L. Adair, Chicago, is again general chairman.

Fellowship in Medicine.—The American College of Physicians offers a limited number of research fellowships, designed to provide an opportunity for research training either in the basic medical sciences or in the application of these sciences to clinical investigation. They are for the benefit of physicians who are in the early stages of their preparation for a teaching and investigative career in internal medicine, pediatrics and other allied fields. Assurance must be provided that the applicant will be acceptable, and the laboratory will supply the facilities necessary for the proper pursuit of the research. The term of appointment is for one year, usually beginning on July 1. The stipend will be from $1,800 to $3,000 a year. Application forms will be supplied on request to the American College of Physicians, 4200 Pine Street, Philadelphia 4, and must be submitted in duplicate, with a recent photograph of the applicant. It is desirable that applications be filed by December 1 each year. Awards will be made on or about January 1. Dr. Reginald Fitz, Boston, is chairman of the committee on fellowships and awards.

Southern Surgical Association.—The fifty-eighth annual session of the Southern Surgical Association, Hot Springs, Va., will be held December 10-12 under the presidency of Dr. Daniel C. Elkin, Atlanta, Ga. Included among the speakers are:

Dr. Winchell McK. Craig, Rochester, Present Status of the Surgical Treatment of Hypertension.
Drs. Elmer C. Bartels and Frank H. Laney, Boston, Use of Thiouracil, Thiobarbital and Propyl Thiouracil in Patients with Hyperthyroidism.
Dr. Richard W. Te Linde, Baltimore, Surgical Treatment of Urinary Incontinence in Women.
Dr. Guy W. Horsley, Richmond, Va., Treatment of Cancer of the Breast in Premenopausal Patients with Radical Amputation and Bilateral Oophorectomy.
Drs. Willard H. Parsons, Vicksburg, Miss., and John S. Harter, Louisville, Ky., Pulmonary Resection for Gangrene of the Lung.
Dr. Frank P. Strickler, Louisville, Ky., True Cavernous Hemangioma of the Uterus.

At the association dinner Wednesday evening Dr. Elkin gave his address entitled "The Georgia Blister and Critic" and Francis Pendleton Gaines, LL.D., president, Washington and Lee University, Lexington, Va., spoke on "Lee: Leader of an Educational Renaissance."

"The Challenge of the Future."—The National Society for Crippled Children and Adults will hold its silver anniversary convention at the Palmer House, December 9-11. The theme of the convention will be "The Challenge of the Future." Among the speakers will be:

Dr. Waldo E. Nelson, Philadelphia, Convalescent Care for the Handicapped.
Dr. Arthur C. Bachmeyer, Chicago, Developments in Hospital Planning of Interest to Workers for the Handicapped.
Dr. Morris Fishbein, Editor, THE JOURNAL, The Medical Care Program of the American Medical Association.
Dr. Alfred R. Shands Jr., Wilmington, Rehabilitation in General Hospitalization.

One general session Wednesday morning, December 11, will be devoted to consideration of the care of the children with cerebral palsy with the following speakers:

Mr. Lawrence J. Linck, Chicago, A National Cerebral Palsy Program.
Jayne Shover, Chicago, Cerebral Palsy Across the Nation.
Dr. Winthrop M. Phelps, Cockeysville, Md., Treatment of Cerebral Palsy.
Dr. Temple S. Fay, Philadelphia, Causal Aspects of Cerebral Palsy.
Dr. Leslie B. Hohman, Baltimore, Assuring Social Acceptance of Cerebral Palsied Children.
Dr. Earl R. Carlson, Pompano Beach, Fla., Educational Needs of the Cerebral Palsied Child.
Dr. Meyer A. Perlstein, Chicago, Recent Advances in Drug Therapy for Cerebral Palsy.
Participation by parents of cerebral palsied children, "As I See It."

Mead Johnson & Company B Complex Award.—Nominations are solicited for the 1947 award of $1,000 established by Mead Johnson and Company to promote researches dealing with the B complex vitamins. The recipient of this award will be chosen by a committee of judges of the American Institute of Nutrition, and the formal presentation will be made at the annual meeting of the institute, May 18-22, 1947. The award will be given to the laboratory (nonclinical) or clinical research worker in the United States or Canada who, in the opinion of the judges, has published during the previous calendar year, January 1 to December 31, the most meritorious scientific report dealing with the field of the B complex vitamins. While the award will be given primarily for publication of specific papers, the judges are given considerable latitude in the exercise of their function. If in their judgment circumstances and justice so dictate, it may be recommended that the prize be divided between two or more persons. It may also be recommended that the award be made to a worker for valuable contributions over an extended period but not necessarily representative of a given year. Membership in the American Institute of Nutrition is not a requisite of eligibility for the award. To be considered by the committee of judges, nominations for this award for work published in 1946 must be in the hands of the chairman of the nominating committee by Jan. 15, 1947. The nominations should be accompanied by such data relative to the nominee and his research as will facilitate the task of the committee of judges in its consideration of the nomination. The chairman is Robert R. Sealock, Ph.D., Department of Chemistry, Iowa State College, Ames, Iowa.

Merck Fellowships in Natural Sciences.—Merck & Co. has established a group of fellowships in natural sciences to be administered by the National Research Council. Not to exceed ten in number, the fellowships are to assist young men and women who have demonstrated ability in research in the chemical and biologic sciences. The fellowships will provide advanced training in these fields. They are open to citizens of the United States who have already acquired the training in chemistry or biology represented by the degree of Ph.D. or its equivalent. The initial appointment will be for a term of one year, renewable for a second, and in exceptional cases for a third. Fellows will be encouraged to undertake their fellowship work in institutions other than those in which their original training has been obtained. The amount of the annual stipend, which will be in the range of $2,500 to $5,000, will be determined by individual circumstances. An allowance for necessary travel will be available in addition. An amount of $500 or more will be provided annually for the institutional expenses of each successful candidate. Applications for Merck Fellowships should be filed by Jan. 15, 1947. Decisions concerning awards will be made as soon as practicable after March 1, 1947. The fellowships will become effective on July 1, 1947. Address communications to the Merck Fellowship Board, National Research Council, 2101 Constitution Avenue, Washington 25, D. C. Members of the Merck Fellowship Board are:

Alfred N. Richards, Ph.D., chairman, University of Pennsylvania School of Medicine.
George W. Beadle, Ph.D., California Institute of Technology.
Hans T. Clarke, D.Sc., Columbia University College of Physicians and Surgeons, New York.
George O. Curme Jr., Sc.D., Carbide and Carbon Chemicals Corporation, New York.
René J. Dubos, Sc.D., Rockefeller Institute for Medical Research, New York.
The chairman, National Research Council, Washington, D. C., ex officio.

Marriages

WALLACE C. WARD, Raleigh, N. C., to Miss LaRene Slater of New Orleans and Apalachicola, Fla., at Charlotte, N. C., August 8.

RAYMOND CRAWFORD RAMAGE, Jacksonville, Fla., to Miss Marguerite G. Taylor in Morristown, Tenn., August 24.

ROBERT N. BROWN, Altadena, Calif., to Miss Rosalie Rumsey of Potterville, Mich., in Glendale, Calif., in September.

EDMUND RHETT TAYLOR, Rochester, Minn., to Miss Mary Baldwin Herbert of Columbia, S. C., September 6.

DALE QUINN FURNELL, St. Paul, to Miss Phyllis Lovaun Jacobson of St. James, Minn., June 15.

EDWARD HENDERSON MCGEHEE to Miss Carolyn Dunn, both of Mobile, Ala., September 10.

CHARLES RICHARD YODER to Miss Edith King, both of Chicago, September 14.

Deaths

Howard Merrill Clute ✠ Brookline, Mass.; Dartmouth Medical School, Hanover, N. H., 1914; born in North Berwick, Maine, January 10, 1890; served as professor of surgery at the Boston University School of Medicine; secretary of the Section on Surgery, General and Abdominal, American Medical Association, from 1932 to 1935, when he was elected chairman; member of the American Surgical Association, Southern Surgical Association, American Society for the Study of Goitre and the Société Internationale de Chirurgie; member and past president of the Boston Surgical Society; fellow of the American College of Surgeons; member of the founders group of the American Board of Surgery; for many years associated with the Lahey Clinic; served as chief of the surgical service at Carney Hospital in South Boston; for many years chief of the surgical service at Massachusetts Memorial Hospitals, where, in recognition of his administrative ability, he was elected to the board of trustees; on the staffs of the Burbank Hospital in Fitchburg, Mass., New England Baptist and New England Deaconess hospitals in Boston; served in the medical corps of the U. S. Army during World War I and was honorably discharged with the rank of major; received the honorary degree of doctor of science from Dartmouth in 1941; died suddenly September 19, aged 56, of coronary thrombosis.

David A. Stanton, High Point, N. C.; Vanderbilt University School of Medicine, Nashville, 1887; born in Level Cross, N. C., May 24, 1859; member of the American Medical Association; honorary member, formerly vice president and secretary of the Medical Society of the State of North Carolina; past president and first secretary of the Guilford County Medical Society; fellow of the American College of Surgeons; served as resident surgeon of the Southern Railway, city health officer, medical director of the Colonial Life Insurance Company, mayor of High Point, member of the board of nursing examiners and state board of health; for many years chairman and treasurer of the city school board; served as city councilman; a charter member of the Perpetual Building and Loan Association, founded in 1901, which he served as first vice president and retired as president to become a member of the board of directors; director of the Pickett Cotton Mills; vice president of the High Point Savings and Trust Company; served on the staffs of the Guilford General Hospital and the High Point Memorial Hospital; died September 5, aged 87, of cardiovascular renal disease.

Sidney Samuel Weinstein, Denver; University of Tennessee College of Medicine, Memphis, 1929; member of the American Medical Association; served as an instructor of pediatrics at the University of Colorado School of Medicine; specialist certified by the American Board of Pediatrics; served on the staffs of the Children's, Beth Israel, Colorado General and Denver General hospitals; began active duty as a lieutenant commander in the medical corps of the U. S. Naval Reserve in October 1942; service terminated Jan. 30, 1946; died September 12, aged 41, of coronary thrombosis.

Oliver Goldsmith Tinkham ✠ Boston; Tufts College Medical School, Boston, 1905; member of the New England Obstetrical and Gynecological Society; fellow of the American College of Surgeons; served as instructor in surgery at his alma mater; on the staffs of the Massachusetts Woman's Hospital, Boston, Newton (Mass.) Hospital and Symmes Arlington Hospital, Arlington; on the associate staff of the New England Baptist Hospital, Boston, and Cambridge Hospital, Cambridge; surgeon, Boston Dispensary and Boston Floating Hospital; died September 10, aged 67, of carcinoma.

Henry Wellington Banks, Norwood, Pa.; Medico-Chirurgical College of Philadelphia, 1902; member of the American Medical Association; died September 24, aged 71.

Eugene Fogle Beard, Somerset, Ky.; University of Louisville Medical Department, 1911; member of the American Medical Association; served during World War I; surgeon for the Southern Railway; died September 19, aged 64, of heart disease.

George Gernon Bergeron ✠ Ludlow, Mass.; Temple University School of Medicine, Philadelphia, 1917; served in France during World War I; school physician; died September 26, aged 55, of carcinoma of the lung.

Alick Bernstein, Chicago; University of Illinois College of Medicine, Chicago, 1916; member of the American Medical Association; died April 4, aged 52.

Leonard Rudolph Boen, Bauxite, Ark. (licensed in Arkansas in 1903); member of the American Medical Association; died at Clarksville September 11, aged 63.

Harry Rich Bolan, Cambridge, Mass.; Middlesex College of Medicine and Surgery, Cambridge, 1915; died September 25, aged 63, of hypertensive heart disease.

Edward Jesse Burnett, Los Angeles; Kansas City (Mo.) Medical College, 1903; died July 18, aged 67.

James Roderick Butler, Mountain City, Tenn. (licensed in Tennessee in 1912); member of the American Medical Association; served as mayor of Mountain City and as county health officer; died September 28, aged 57, of carcinoma.

L. D. Carter, West Liberty, Ky.; Kentucky School of Medicine, Louisville, 1882; died in Lexington September 24, aged 92.

Jediah Hussey Clark, Winter Park, Fla.; Medical College of Indiana, Indianapolis, 1895; past president of the Fayette-Franklin Counties (Ind.) Medical Society; served as secretary of the board of health of Connersville, Ind.; killed in an automobile accident near Macon, Ga., September 22, aged 77.

Bernard L. Cleary, Edgerton, Wis.; Rush Medical College, Chicago, 1900; died in the Edgerton Memorial Hospital September 21, aged 76, of carcinoma of the bladder and prostate.

Joseph Wilmer Cox, Groesbeck, Texas; Medical Department of Tulane University of Louisiana, New Orleans, 1893; fellow of the American College of Surgeons; chief examiner, Limestone County Selective Service Board; medical director and owner of Dr. Cox's Hospital; died September 17, aged 78, of bronchopneumonia.

George S. Cressman, Pughtown, Pa.; University of Pennsylvania Department of Medicine, Philadelphia, 1890; member of the American Medical Association; died September 26, aged 77, of Parkinson's disease.

William Ray Day, Fairfield, Iowa; Keokuk Medical College, College of Physicians and Surgeons, 1901; died September 19, aged 80, of leukemia.

Louis Sharpe Dunaway, Jr. ✠ Conway, Ark.; University of Arkansas School of Medicine, Little Rock, 1929; served as a captain in the medical corps, Army of the United States, during World War II; died September 18, aged 46, of lymphosarcoma.

Welcome McClellan Elwell, Toledo, Ohio; Starling Medical College, Columbus, 1890; died September 29, aged 82, of cerebral hemorrhage.

Ernest Emory Esley, Walworth, N. Y.; Cleveland Homeopathic Medical College, 1902; member of the American Medical Association; served as health officer and fire commissioner; associate staff member of the Genesee Hospital in Rochester, where he died September 28, aged 76, of arteriosclerotic heart disease.

Albert S. Faulkner, Waynetown, Ind.; University of Louisville (Ky.) Medical Department, 1893; member of the American Medical Association; died September 25, aged 76, of cerebral hemorrhage.

Frank M. Gaines, Verden, Okla.; Kentucky School of Medicine, Louisville, 1894; died in August, aged 86.

Albert William Glathar ✠ Pueblo, Colo.; University of Nebraska College of Medicine, Omaha, 1929; diplomate of the National Board of Medical Examiners; past president and secretary of the Pueblo County Medical Society; on the staffs of the Parkview Hospital and St. Mary's Hospital, where he died September 27, aged 45, of mycosis.

Frederick George Graves ✠ Bethlehem, Conn.; Yale University School of Medicine, New Haven, 1892; past president of the Connecticut State Medical Society; died September 23, aged 77.

Harry Gus Greditzer, St. Louis; Washington University School of Medicine, St. Louis, 1912; member of the American Medical Association; on the staff of the Jewish Hospital; died September 27, aged 56, of coronary occlusion.

Charles Michael Hauslein, Omaha; Rush Medical College, Chicago, 1900; died in the Immanuel Hospital September 8, aged 73, of heart disease.

William Herbert Ingram, Pittsburgh; Western Pennsylvania Medical College, Pittsburgh, 1894; served as professor of pathology, bacteriology and histology at his alma mater, now known as the University of Pittsburgh School of Medicine; died July 4, aged 77, of cerebral hemorrhage.

Lawrence Leslie Irwin, Bloomington, Ill.; St. Louis University School of Medicine, 1907; member of the American Medical Association; on the staff of St. Joseph's Hospital, where he died September 17, aged 60, of cerebral hemorrhage.

Harry Breckenridge Jacobson, Dallas, Texas; Tulane University of Louisiana School of Medicine, New Orleans, 1918; member of the American Medical Association; died in Gaston Hospital August 31, aged 54, of congestive heart disease.

Maurice Kemp ✠ Allentown, Pa.; Cornell University Medical College, New York, 1907; past president of the Lehigh Valley Medical Society; served during World War I and as examining physician for the induction center during World War II; died September 24, aged 60.

Clarence Perry Kummer ✠ Buffalo; University of Buffalo School of Medicine, 1917; served during World Wars I and II; member of the American Heart Association; on the staff of the Deaconess Hospital; died September 16, aged 52, of coronary occlusion.

William Leonard, Fostoria, Ohio; Western Reserve University Medical Department, Cleveland, 1888; served during World War I; died September 23, aged 84, of heart disease.

Harold L. Lorentzen, Petaluma, Calif.; Hahnemann Hospital College, San Francisco, 1900; College of Physicians and Surgeons of San Francisco, 1902; died in a hospital at Santa Rosa September 6, aged 81, of bronchopneumonia, Parkinson's disease and arteriosclerosis.

Frank Mansfield Loring, Howard, S. D.; University of Michigan Department of Medicine and Surgery, Ann Arbor, 1885; died September 6, aged 85.

S. J. McGraw, El Dorado, Ark.; University of Arkansas School of Medicine, Little Rock, 1906; member of the American Medical Association; served as city and county health officer; died in the Warner Brown Hospital September 6, aged 72, of coronary thrombosis.

James Alexander MacKenzie, Boston; Tufts College Medical School, Boston, 1913; died September 16, aged 68, of heart disease.

George Ralph Maner ✠ Tampa, Fla.; University of Georgia Medical Department, Augusta, 1893; on the courtesy staff of the Tampa Municipal Hospital; died July 23, aged 74, of coronary occlusion.

Harrie Breckinbridge Martin, Springfield, Ohio; University of Pennsylvania Department of Medicine, Philadelphia, 1903; for many years affiliated with the Springfield City Hospital; died September 1, aged 68, of heart disease.

Patrick Joseph O'Dea, Fitchburg, Mass., University of Vermont College of Medicine, Burlington, 1912; member of the American Medical Association; died September 25, aged 59, of coronary sclerosis.

Frederick E. Pierce, Chicago; National Medical College, Chicago, 1897; served on the school board and city council of Earlville, Ill.; died September 27, aged 85.

Capt. Joseph C. Bulfamonte
M. C., A. U. S., 1907-1946

Robert Pierson Regester, Philadelphia; Jefferson Medical College of Philadelphia, 1916; died in the U. S. Naval Hospital June 8, aged 54, of hypertensive cardiovascular disease.

Thomas McPherson Roberts, Sweetwater, Tenn.; Kentucky School of Medicine, Louisville, 1894; member of the American Medical Association; died in the Sweetwater Hospital September 14, aged 77, of carcinoma of the liver.

Henry Joseph Rock, Wilmington, Del.; College of Physicians and Surgeons of Chicago, School of Medicine of the University of Illinois, 1900; member of the House of Delegates of the American Medical Association in 1904, 1907 and 1908; served as mayor of Aberdeen, S. D., where he was on the staff of St. Luke's Hospital; died September 9, aged 82, of cerebral hemorrhage.

Bertha May Satterlee, Bellevue, Ohio; Cleveland Medical College, 1894; died September 2, aged 78.

George Louis Schneider ✠ Williamsport, Pa.; Jefferson Medical College of Philadelphia, 1911; fellow of the American College of Surgeons; past president of the Lycoming County Medical Society; served as county coroner; on the staff of the Williamsport Hospital, where he died September 17, aged 60, of coronary thrombosis.

Ralph Levi Souder, Philadelphia; Hahnemann Medical College and Hospital of Philadelphia, 1896; died July 23, aged 74, of cerebral hemorrhage.

Trond Neilson Stabo ✠ Decorah, Iowa; Kongelige Frederiks Universitet Medisinske Fakultet, Oslo, Norway, 1894; died in Hayward, Wis., August 20, aged 76, of heart disease.

Allison A. Stamm, Mohnton, Pa.; University of Vermont College of Medicine, Burlington, 1883; member of the American Medical Association; died July 21, aged 90, of arteriosclerosis.

Oscar Blue Swayze, Auburn, N. Y.; Long Island College Hospital, Brooklyn, 1892; member of the American Medical Association; served on the staffs of the Mercy and Auburn City hospitals; died September 4, aged 82, of arteriosclerosis.

William Joshua Groot Thomas, Washington, D. C.; George Washington University School of Medicine, Washington, D. C., 1908; served during World War I; on the staffs of the Sibley Hospital and the Garfield Memorial Hospital, where he died September 22, aged 71, of cerebral thrombosis and diabetes mellitus.

Payne Alexander Tinsley, Dandridge, Tenn.; University of Louisville (Ky.) Medical Department, 1895; died September 5, aged 80, of heart disease.

Henry B. Trigg, Fort Worth, Texas; Fort Worth School of Medicine, Medical Department of Fort Worth University, 1904; member of the American Medical Association; at one time on the faculty of his alma mater; died in a local hospital September 12, aged 66.

Karl William Wahlberg ✠ Moline, Ill.; Rush Medical College, Chicago, 1912; past president of the Rock Island County Medical Society; past president and vice president of the Iowa and Illinois Central District Medical Society; served during World War I; on the staffs of the Moline Public and Lutheran hospitals; died September 29, aged 59, of myocardial infarction.

Armon French Wicks, Okolona, Miss.; College of Physicians and Surgeons, Memphis, Tenn., 1911; awarded the Purple Heart and Silver Star for service overseas during World War I; died in Memphis, Tenn., September 19, aged 66.

Benjamin A. Wilkes, North Hollywood, Calif.; Hospital College of Medicine, Louisville, 1882; served as president of the American Protestant Hospital Association; formerly superintendent of the Missouri Baptist Hospital in St. Louis and the Southeast Missouri Hospital in Cape Girardeau, Mo.; served as superintendent of the Hollywood Clara Barton Memorial Hospital in Los Angeles; died September 18, aged 88.

Ernest G. Wilson ✠ Kankakee, Ill.; Indiana Medical College, School of Medicine of Purdue University, Indianapolis, 1906; served on the staff of St. Mary Hospital; died September 25, aged 61, of coronary thrombosis.

Frederick Newton Winans, Franklin, N. Y.; College of Physicians and Surgeons, medical department of Columbia College, New York, 1874; member of the American Medical Association; life member of the Otsego County Medical Society; for many years served as health officer, president of the board of trustees of the Delaware Literary Institute and as village president; honorary member of the staff of the Sidney (N. Y.) Hospital; died September 21, aged 95, of senility.

Charles Henry Wyatt ✠ Kansas City, Mo.; University of Arkansas School of Medicine, Little Rock, 1931; interned at the Kansas City General Hospital, where he was a member of the staff; served on the staff of the Research Hospital, where he died September 15, aged 42, of acute hemorrhagic pancreatitis.

KILLED IN ACTION

Joseph Charles Bulfamonte ✠ Philadelphia; Georgetown University School of Medicine, Washington, D. C., 1932; interned at the Philadelphia General Hospital; served a residency at the Norristown State Hospital in Norristown, Pa., and the Ashland State Hospital in Ashland, Pa.; served on the staff of the Shamokin (Pa.) Hospital; began active duty as a first lieutenant in the medical reserve corps of the U. S. Army on April 19, 1941; later promoted to captain in the medical corps, Army of the United States; prisoner of war in the Philippine Islands; presumed dead March 14, 1946, aged 39.

Foreign Letters

PARIS

(From Our Regular Correspondent)

Nov. 15, 1946.

Sanitary Condition of France

The present minister for public health is the last provisory minister of the present government of France. The poll of the 10th of November will establish for five years a new parliament and a long term government. The minister in a statement on his activity during this short period, read at a press conference, gave some insight on the sanitary condition of the country. He had to direct his efforts toward the solution of numerous urgent problems. A census of the hospital appliances has been taken and a scheme of reequipment, giving priority to war devastated "Départements" has been established. Reconstruction work has began at Nantes and Toulon; at Lorient and Brest the hospital system has been reestablished; at Rouen, Rennes, Rheims and Nancy the U. S. Army has given the hospitals back to the civil sanitary services. The second examination of the deported and prisoners having shown an increase in cases of tuberculosis, several new sanatoriums, among which is one in the Black Forest, in the French occupation zone, have been opened and numerous radiology cars have been bought. The working of the sanitary control at the frontiers has been reinforced and a sanitary team is in action at the Marseilles-Marignane air port; similar ones are being organized at Le Bourget and Orly. The first 600,000 sanitary books to be used for newborn children have been distributed. The circular of the 3d of September has created a section of sanitary education in each district. Penicillin, which, up to the present moment, was used only in special centers, is now available for every doctor. The Information Bulletin of the Ministry for Public Health contains a favorable statement of the epidemic condition of France last summer: Apart from the poliomyelitis epidemic, which is declining, two localized epidemics of typhoid and paratyphoid and some cases of Weil's disease have been reported.

Special circulars have ordered the reorganization of the psychiatric equipment and of the antituberculosis organizations. Laws concerning the protection of mothers and children have been promulgated and are in course of realization. The weak points, pointed out by the minister, are a delay in the modernization of equipment in hospital appliances, due to the war and Nazi occupation, and backwardness in the field of anesthesia, due to the impossibility of taking part in international congresses.

Several missions for study have been sent to the United States, Great Britain and Russia. There is a shortage of certificated nurses and district nurses; also a lack of cars for doctors and especially for country doctors; in order to make up for it army cars will be allotted to them. In order to avoid the parallelism of the activities of the Ministries for Public Health and of Social Security in the planning of the organization of the hospital system, an interministerial commission of coordination has been appointed. In the organization of the sanitary service, decentralization will be maintained: in each city of more than 20,000 inhabitants a municipal bureau of hygiene will be created and the power of the mayor, as regards public hygiene and sanitary police, will be increased. In every center of more than 10,000 inhabitants the establishment of "goutte de lait" (the drop of milk) organization for the supervision and the repartition of wholesome milk is foreseen as well as, in each department, the creation of a committee for the protection of unadopted children. A detailed plan for departmental public schools for nurses and district nurses is also completed and will be presented to the future parliament. The creation of sanitary "attachés" to the embassies in China, the United States and Russia are foreseen for 1947.

OSLO

(From a Special Correspondent)

Nov. 11, 1946.

Airplane Flights for Whooping Cough

The somewhat bizarre treatment of the intractable cough of whooping cough patients by sending them for a spin in an airplane does not seem to be remarkably successful. Inquiries recently addressed to the mothers of these patients sent aloft at the Fornebu airdrome near Oslo yielded the information that in 9 out of 33 cases improvement was noted from two to fourteen days after the flight. In most cases no improvement was effected, and all the parents achieved was the expenditure of 60 to 90 kroner for the flights and the exposure of their children to the risks incidental to flying. Dr. Alf Ödegaard, who has collected these data by interviewing the parents, has found little reason for recommending this treatment as a safe and rational procedure.

Diabetes Mellitus in Bergen

Dr. Per Hanssen of the staff of Ullevaal Hospital has published a study of diabetes in Bergen, the population of which is about 100,000. The object was to investigate the morbidity, age at onset, duration and the most frequent complications of diabetes, as well as the causes of death since the introduction of insulin treatment. He finds that, since the introduction of this treatment, it has become increasingly necessary to distinguish between deaths from diabetes and deaths from other causes in diabetic patients. To this end he suggests that in the future a distinction should be made between the two in the official notifications of death. The observations of Joslin and his fellow workers are made by Dr. Hanssen to serve as a background for his own investigations, which in more than one instance show that the behavior of diabetes is by no means the same in different countries.

The Shock Treatment of Psychoses in Norway

Dr. H. H. Dedichen, in charge of the private asylum associated with his name near Oslo, has completed a study of the shock treatment of psychoses as practiced in various Norwegian asylums. This 160 page study, issued by the Danish publisher Ejnar Munksgaard in 1946, covers a period of several years and deals with material collected in seventeen different asylums. In the autumn of 1938 Dr. Dedichen enlisted the cooperation of the medical superintendents of these asylums, many of which have also provided valuable control material. Altogether, 1,459 shock treated patients were compared with 969 comparable patients not given such treatment. Throughout this study Dr. Dedichen shows himself acutely conscious of the many pitfalls awaiting any one undertaking such a comparison, and he has taken special pains in matching the psychoses of the treated and not treated patients. One of his important conclusions is that the benefits of shock treatment are greatest and most effectively demonstrable when the duration of the mental disease in question has been less than one year before the institution of this treatment.

Heredopathia Atactica Polyneuritiformis

Dr. Sigvald Refsum, on the staff of the Neurologic University Clinic in Oslo, has published a comprehensive study of a familial syndrome which has not hitherto been described. This syndrome appeared in two Norwegian families not related to each other and living in two widely separated districts in Norway. Hemeralopia was observed in all 5 patients and atypical retinitis pigmentosa in 3 members of one family. In 2 members of the other family there were reasons to suspect this condition or a similar condition without pigmentation. Other characteristics of the syndrome were suggestive of chronic polyneuritis and ataxia. There were also certain other cerebellar phenomena.

Correspondence

IMPORTANCE OF BLOOD GROUP TESTS

To the Editor:—In the October 19 issue of THE JOURNAL an editorial comment stressed the value of blood tests for identification, especially in relation to blood samples and stains obtainable at postmortem examination. The article urged that "provision should be made to collect and save samples of blood at necropsies for eventual blood group tests much more regularly than is now the usual practice."

I should like to suggest another important place for complete blood grouping as a means of identification where mistaken identity has often caused much anguish and has even made history, namely in the delivery room. Nowadays most hospitals take prints of the mother's thumb and of the newborn infant's foot as a means of identification. Usually either or both prints are smudged beyond recognition and are worthless. Even if the prints are taken carefully, they soon become useless because the baby's foot pattern, unlike that of an older child, or adult, changes after a few months and cannot be duplicated.

Employing blood groups in identification of the newborn child would be far more useful because they are permanent and can always be duplicated. Furthermore, the blood sample can be obtained from the umbilical cord, thus identifying the child even before it leaves the mother's side for its first bassinet. This sample of blood, oxalated, in a corked tube of suitable size, can easily be fastened to the mother's body, thus preventing separation of the baby's means of identification from its mother during her transfer to her postpartum bed.

With the six blood groups and subgroups (O, A_1, A_2, B, A_1B and A_2B), the three MN types (M, N and MN), the agglutinogen P (P+ and P—) and the ten Rh-Hr types, 360 varieties of human blood can be differentiated. Surely, the chance of incorrectly identifying a baby in this way is far smaller than by means of a smudgy footprint which could not be duplicated in the event that the identity of the child should be questioned a few months after birth.

Admittedly, identification of babies through the medium of blood groups demands reasonable knowledge of grouping tests and of the use of the various testing serums, but, since such knowledge can be obtained and since all the necessary serums are becoming more readily available, there is no great or insurmountable obstacle in the path of its development.

MALCOLM A. HYMAN, M.D.,
Blood Transfusion Service,
Jewish Hospital of Brooklyn,
Brooklyn.

PENICILLIN INHALATION

To the Editor:—Reading the report on Penicillin Inhalation by Morse in THE JOURNAL October 5 and the editorial in the same issue on Penicillin Aerosol Therapy prompted me to suggest that a review of the literature on this subject would have provided a more dependable guide for the dosage, technic and results of the use of penicillin by inhalation.

Morse's observations on 25 patients with various types of upper respiratory complications seen during an influenza epidemic unfortunately lack evidence to support the statement that the dosage required by this method is less than that needed by intramuscular injections for the management of pulmonary infection. He employed a hand bulb nebulizer technic which produces coarse sprays, probably deposited largely in the oropharynx, trachea or larger bronchi. Small doses totaling 14,000 to 80,000 units of penicillin were given daily in four divided doses for two to four days. He stated "I have always used 4 drachms (15 cc.) in twenty-four hours." Referring to his most concentrated dilution, this would mean about 16,000 units in 4 cc. of solution for each treatment. This would require considerable hand pumping during an allotted ten minute period! Certainly such a technic is hardly feasible for a sick patient. This small dosage might possibly be valuable in the variety of milder respiratory complaints in his patients but would be entirely inadequate and dangerous for the control of the types of bronchopulmonary infections best managed by penicillin aerosol therapy.

Effective penicillin aerosol therapy can provide good topical effect as well as adequate blood levels. In 118 determinations I obtained blood levels which ranged from 0.015 to 0.225 unit per cubic centimeter with doses of 25,000 to 50,000 units. My studies and those by Barach and Olsen have repeatedly indicated the need for adequate doses, ranging from 200,000 to 500,000 units daily, for the satisfactory control of most bronchopulmonary infections. The saving in penicillin should not be used as an argument for employing this method.

The administration of penicillin by inhalation for respiratory infections is more than empirical therapy. A number of patients with lung abscess, bronchiectasis and nonpneumococcic pneumonias had received intramuscular penicillin and oral sulfonamides without demonstrated improvement before getting penicillin aerosol which resulted in cure. However, it does have a limited field of usefulness and should be employed only when definitely indicated and then with an effective technic. Such therapy is mainly indicated for patients having purulent sinusitis, bronchiectasis and lung abscess, especially in the presence of streptococcus, staphylococcus, pneumococcus or penicillin-susceptible strains of Friedländer's infections of the lungs and acute infectious laryngotracheobronchitis. In chronic bronchitis, bronchial asthma and pulmonary emphysema penicillin aerosol may or may not be preferable to systemic penicillin administration but it has been found equally beneficial. Every attempt should be made to identify the organisms from the nose, throat and sputum and, if possible, to determine the penicillin sensitivity before instituting adequate therapy.

MAURICE S. SEGAL, M.D., Boston.

Medical Motion Pictures

FILM REVIEW

Vaginal Flora During Pregnancy. 16 mm., color, silent, 790 feet, showing time twenty-two minutes (run at sound speed). Prepared in 1946 and procurable from A. Herbert Marbach, M.D., 1022 Medical Arts Building, Philadelphia.

A motion picture showing normal and abnormal flora during pregnancy with associated p_H changes. Gross changes of the vagina are also illustrated. An elaborate scientific film based on vaginal cultures made through a sterile tube introduced in the vagina, through which is passed a swab used for the culture.

This picture requires considerable knowledge of bacteriology. Parts, such as the preparation of the hands in order to make these cultures, are overdone. The film requires additional explanatory titles in order that the average physician may fully appreciate its practical value. The type of audience recommended includes gynecologists, medical students, interns and residents.

The film possesses educational value and should be repeatedly shown to establish knowledge of the complicated bacterial flora of the vagina.

The color photography is well done.

Bureau of Investigation

MISBRANDED PRODUCTS

Abstracts of Notices of Judgment Issued by the Food and Drug Administration of the Federal Security Agency

[EDITORIAL NOTE.—These Notices of Judgment are issued under the Food, Drug and Cosmetic Act, and in cases in which they refer to drugs and devices they are designated D.D.N.J. and foods, F.N.J. The abstracts that follow are given in the briefest possible form: (1) the name of the product; (2) the name of the manufacturer, shipper or consigner; (3) the date of shipment; (4) the composition; (5) the reason for the charge of misbranding, and (6) the date of issuance of the Notice of Judgment.]

Asthma Tea.—Manning Herb House, Bessemer, Ala. Shipped March 30, 1942. Composition: essentially roughly ground plant material, identity not reported. Misbranded because label falsely represented product as efficacious in preventing, curing or treating asthma, and because label misstated quantity of contents.—[*D. D. N. J., F. D. C. 1043; March 1945.*]

Balm and Gilead Herb Tonic.—Manning Herb House, Bessemer, Ala. Shipped March 30, 1942 Composition: plant drug extractives (no alkaloids), a small amount of gum resin, reducing sugar, and water. Misbranded because labeling falsely represented it as helpful for asthma cough and chronic cough, and as a tonic for these conditions.—[*D. D. N. J., F. D. C. 1043; March 1945.*]

Brom-Acet.—Purity Drug Company, Inc., New York. Shipped June 18 and 23 and July 11, 1942. Composition: from 10.4 to 11.9 grains of sodium bromide per ounce, whereas label claimed 16 grains of this substance per ounce. Hence adulterated and misbranded.—[*D. D. N. J., F. D. C. 1022; March 1945.*]

Blood and Liver Capsules. — Manning Herb House, Bessemer, Ala. Shipped March 30, 1942. Composition: mercury (about 10 per cent) and black pepper reported. Misbranded because falsely represented to remedy disorders of blood, liver, stomach and bowels.—[*D. D. N. J., F. D. C. 1043; March 1945.*]

Blood Tonic.—Manning Herb House, Bessemer, Ala. Shipped March 30, 1942. Composition: plant debris (not identified), water-soluble plant extractives, and water, with a foul odor suggesting burdock or Jimson weed. Misbranded because title falsely represented article as a tonic—[*D. D. N. J., F. D. C. 1043; March 1945.*]

Cel-Bio Mineral Tablets. — Cel-Bio Mineral Food Company, Omaha. Shipped May 7 and 8, 1942. Composition of all tablets, numbered from 1 to 12, essentially lactose with a minute amount of a different mineral in each. All misbranded because of label misrepresentations as to their effects on various disorders.—[*D. D. N. J., F. D. C. 1042; March 1945.*]

Codecol.—Harvey Laboratories, Inc., Philadelphia. Shipped Sept. 22 and Dec. 12, 1942. Composition: not more than 6.73 grains of ammonium chloride or 0.1 grain of antimony potassium tartrate per fluid ounce, whereas falsely represented to contain larger amounts, and hence adulterated and misbranded.—[*D. D. N. J., F. D. C. 1017; March 1945.*]

Colusa Natural Oil, Colusa Natural Oil Capsules and Colusa Natural Oil Hemorrhoid Ointment.—Colusa Products Company, Berkeley, Calif. Shipped Jan. 31, 1941. Composition: the two first-named products consisted of crude petroleum oil, containing 0.75 per cent of sulfur, but not the camphor, turpentine, iodine or iodine compounds declared on label. Ointment was essentially zinc oxide, crude petroleum oil and small amounts of camphor, menthol and benzocaine in a base of lanolin and beeswax. Oil and Capsules misbranded because label falsely represented them as efficacious in treating eczema, psoriasis, acne, ringworm, athlete's foot, poison ivy, varicose ulcers and some other conditions; Ointment misbranded because label falsely represented it as efficacious in treating hemorrhoids.—[*D. D. N. J., F. D. C. 1040; March 1945.*]

"For Nervous Run Down Women."—A product of this name was sold by the Manning Herb House, Bessemer, Ala. Shipped March 30, 1942. Composition: essentially a small amount of plant debris (type not reported), water-soluble plant extractives and water. Misbranded because name falsely represented that the product would benefit nervous, run-down conditions in women.—[*D. D. N. J., F. D. C. 1043; March 1945.*]

Hart's Vitamin B Elixir.—E. J. Hart & Company, Ltd., New Orleans. Shipped June 8, 1942. Adulterated and misbranded because product contained only 13.8 milligrams of nicotinic acid per fluid ounce instead of the 20 milligrams falsely declared on label.—[*D. D. N. J., F. D. C. 1029; March 1945.*] Also declared adulterated and misbranded under the provisions of the law applicable to foods, as reported in *F. N. J. 5775.*

Kaps Colloidal Iodized Sulphur.—Jamco Company, New York. Shipped June 5 and Aug. 27, 1942. Composition: capsules containing mineral oil, sugar, small amounts of sulfur, and an iodide. Misbranded because label statement, "For use as an aid in the relief of arthritis due to sulphur deficiency," falsely represented product as effective for arthritis.—[*D. D. N. J., F. D. C. 1046; March 1945.*]

Manning's Asthma Plaster. — Manning Herb House, Bessemer, Ala. Shipped March 30, 1942. Composition: essentially dry ground mustard and ground black pepper. Misbranded because name falsely suggested usefulness for asthma.—[*D. D. N. J., F. D. C. 1043; March 1945.*]

Manning (D. R.) Antiseptic Douche Powder.—Manning Herb House, Bessemer, Ala. Shipped March 30, 1942. Composition: essentially 4 parts of boric acid to 1 of oxyquinoline sulfate. Misbranded because falsely represented that when diluted according to directions it was an antiseptic and efficacious as a douche for feminine hygiene.—[*D. D. N. J., F. D. C. 1043; March 1945.*]

Manning (D. R.) Asthma Salve.—Manning Herb House, Bessemer, Ala. Shipped March 30, 1942. Composition: essentially petrolatum, with a small amount of volatile oils, including menthol, eucalyptol and camphor. Misbranded because falsely represented on label as efficacious for head colds, headache, catarrh, hay fever, asthma and sinus disorders.—[*D. D. N. J., F. D. C. 1043; March 1945.*]

Manning (D. R.) Throat Gargle.—Manning Herb House, Bessemer, Ala. Shipped March 30, 1942. Composition: essentially plant material, probably of citrus and pineapple origin, and water, preserved with sodium benzoate. Misbranded because label falsely represented that product was an adequate treatment for sore, inflamed or hoarse throat and would remove goiter.—[*D. D. N. J., F. D. C. 1043; March 1945.*]

Manning's Princess Gaynell Hair Tonic. — Manning Herb House, Bessemer, Ala. Shipped March 30, 1942. Composition: a small amount of plant debris, with odor of cardamom or lavender. Misbranded because label falsely represented that product was a food or fertilizer for the hair, would feed the roots and act as a tonic for the hair.—[D. D. N. J., *F. D. C. 1043; March 1945.*]

Nakamo Bell Tablets. — Hollings-Smith Company, Orangeburg, N. Y. Shipped Nov. 20, 1942. Composition: in each tablet essentially 2 grains of ammonium chloride, 3 grains of sodium chloride and 1 grain of potassium chloride. Misbranded because label falsely represented efficacy of product in treating hay fever, sinusitis, asthma and colds.—[*D. D. N. J., F. D. C. 1045; March 1945.*]

Pantabee. — Charles C. Haskell & Company, Inc., Richmond, Va. Shipped Jan. 13, 1943. Composition: not more than 250 International units of vitamin B_1 per capsule, whereas strength was given as 333 International units on label. Hence adulterated and misbranded.—[*D. D. N. J., F. D. C. 1027; March 1945.*] Also adulterated and misbranded under provisions of the law applicable to foods, as reported in *F. N. J. 5774.*

Py-Ro.—Oran Products, New York. Shipped April 3, 1943. Composition: essentially sodium hypochlorite, chlorthymol, and oil of peppermint dissolved in water. Misbranded because name and label suggestions falsely represented the product as an effective treatment for pyorrhea and trench mouth.—[*D. D. N. J., F. D. C. 1089; April 1945.*]

Rheumatox.—Rheumatox Company, Cleveland. Shipped April 20 and July 15, 1942. Composition: essentially an aqueous solution of sodium salicylate, methenamine, potassium citrate, potassium iodide, emodin-bearing drugs, and a small amount of alcohol. Misbranded because name of product and firm would give erroneous impression that Rheumatox would cure, prevent or mitigate rheumatism; because label falsely represented that excess uric acid commonly causes arthritis, neuritis, lumbago, sciatica, rheumatic pains and gout, and that Rheumatox would prevent or cure these conditions, and because label failed to declare presence of potassium iodide, an active ingredient.—[*D. D. N. J., F. D. C. 1044; March 1945.*]

Sun-Glow Cod Liver Oil Concentrate Tablets.—Brewer & Company, Inc., Worcester, Mass Shipped July 15, 1941. Misbranded because labeling misstated content of vitamins A and D and falsely represented product as efficacious in preventing and treating disease by increasing general resistance, toning the system and developing strong bones and good teeth.—[*D. D. N. J., F. D. C. 1013; March 1945.*] Also adulterated and misbranded under provisions of the law applicable to foods, as reported in *F. N. J. 6597.*

Swiftide Brand Cod Liver Oil.—Swiftide Company, Portland, Maine. Shipped Feb. 7 and April 4, 1942. Adulterated and misbranded because quality fell below standard set for cod liver oil by the United States Pharmacopeia.—[*D. D. N. J., F. D. C. 1015; March 1945.*]

Vigor 8.—Royal Products Company, Chicago. Shipped March 23, 1944. Composition: dried brewers' yeast, corn flour, and corn and wheat germs. Misbranded because labels, as well as "Charles D. Kasher's Health and Beauty Chart" which accompanied product, falsely represented that article was of significant nutritional value in that it contained factors of brewers' yeast, and the elements potassium, sulfur, sodium, magnesium, copper, zinc, chlorine and manganese, and that use of Vigor 8 would prevent or correct many disorders, such as cold infection, ulceration, stone formation, cystitis, paralysis, cataract, scurvy and diabetes.—[*D. D. N. J., F. D. C. 1078; April 1945.*] Also declared misbranded under provisions of the law applicable to foods, as reported in *F. N. J. 6591.*

Whoa Liniment. — Manning Herb House, Bessemer, Ala. Shipped March 30, 1942. Composition: essentially an inflammable hydrocarbon capable of ignition with red hot metal, and containing mustard oil and camphor. Misbranded because falsely represented as an adequate treatment for arthritis, lumbago, sciatica and kindred disorders.—[*D. D. N. J., F. D. C. 1043; March 1945.*]

Bureau of Legal Medicine and Legislation

MEDICOLEGAL ABSTRACTS

Malpractice: Failure to Remove Gauze Packing From Antrum.—The plaintiff sought to recover damages for the loss of an eye, alleged to have been caused by the defendant's failure to remove a piece of gauze packing from the plaintiff's antrum for approximately five months after a surgical operation. The jury returned a verdict of $20,000, it being specified that $10,000 was "for loss of sight of her eye." The court entered judgment for the plaintiff for $10,000, it being of the opinion that there was no evidence that the alleged negligence was the proximate cause of the loss of the eye. Both parties appealed to the Supreme Court of Oregon.

In July 1940 the plaintiff consulted the defendant, a surgeon of some thirty-five years' experience, relative to a growth or cyst on the inside of her nose which x-ray pictures showed to be a tumor of the antrum. Surgery was recommended and an operation performed in October 1940. During the operation a specimen of tissue was submitted to Dr. Robertson, a pathologist, and his report showed that the plaintiff had a basal cell type of cancer—i. e., a low grade cancer which had invaded the bone or roof of the antrum. The cancer was removed and, in view of the pathologic report, the operation was more extensive than had been anticipated, it being necessary to remove much of the channel bone between the antrum and the nose and some of the bone constituting the roof of the antrum, which is also the floor of the orbital cavity. The defendant testified in effect that, since the cancerous cells were ascending in the bone of the antrum, he removed some of the bone but did not go into the orbital cavity on account of the serious consequences to the eye and cheek bone. Later it was decided to use radium to kill the remainder of the cancer cells. Defendant admitted having used gauze packing in the operation but asserted positively that it was removed when the operation was completed. He was corroborated in this respect by other witnesses who assisted him.

Subsequently Dr. Wight, a specialist in radium therapy, inserted a 0.50 milligram radium capsule in plaintiff's antrum and left it there for a period of forty-eight hours. Dr. Wight testified that, when this treatment was completed, the capsule and gauze packing surrounding the same were removed in the presence of the defendant and that the antrum was then free of any gauze packing. Dr. Wight explained the nature of radium therapy and stated that its rays would kill not only cancer cells but also other cells and tissue within a certain radius. It was his opinion that the radium treatment would not only damage the bone of the orbital cavity but would probably result in the loss of the eye. The testimony shows that cancer of the antrum is rare and the rate of mortality in such cases is extremely high. Therefore it is fair to assume that the defendant and his assistants were primarily concerned with curing the cancer, since, if the cancer was not cured, the loss of the eye would be of secondary importance. For the few months following the radium treatment the plaintiff was in and out of the hospital, her condition becoming progressively worse. The antrum was irrigated and treated by x-ray. The eye was in a serious condition at this time, necrosis of the bone having progressed rapidly, and there was a profusion of foul pus. The defendant said that he may have used gauze packing during this period of treatment to aid in drainage of the pus.

After leaving the hospital, plaintiff called regularly at the office of Dr. Fenton, an eye, ear, nose and throat specialist, for treatment of her eye. On March 1 Dr. Fenton looked into the antrum, which is about the size of a large walnut, "to see whether there were any fragments of bone which might be loose" as a result of the radium treatment and then discovered a piece of gauze packing ½ inch wide and 4 or 5 inches long. It was "wadded up pretty solid, because it was packed in there tight" and was covered with pus having a "terrible odor." The defendant had not informed him about the gauze packing and he was very much surprised to find it. The plaintiff desired the piece of gauze to show Dr. Pettit but "Dr. Fenton very properly ordered it destroyed." Plaintiff said that, after the gauze was removed, she was able to breathe again through the left nostril. Dr. Fenton, in response to a hypothetical question, testified that it was not proper practice thus to leave a piece of gauze packing in the operative area for a period of five months "or thereabouts." On March 5 Dr. Fenton removed plaintiff's left eye. He said that at that time "there was no cancer, it had all been killed." It was his opinion that the loss of the eye was caused by the radium and not by the infection resulting from the gauze packing. This conclusion as to the cause of the loss of the eye was supported by all the other medical experts, with the exception of one who testified on behalf of the plaintiff.

The only expert witness who testified on behalf of the plaintiff was a Dr. Nelson, who examined the plaintiff in the latter part of March in order to qualify as an expert witness. He testified, among other things, "I don't believe there ever was a cancer there" and that he did not believe in radium or x-ray therapy for treatment of cancer, although he confessed to never having used the same in his practice. On direct examination, in response to a hypothetical question, Dr. Nelson stated positively that the gauze packing was the cause of the loss of the eye and that radium had nothing to do with it. On cross examination, however, he testified, in answer to a question as to what damage would the radium do, "Well it would destroy the eye in that condition—in that place."

Has it been established with reasonable certainty that leaving the gauze packing in the plaintiff's antrum was the cause of the loss of her eye, the Supreme Court asked, or was such damage caused by the radium treatment? The evidence viewed in the light most favorable to plaintiff is that the loss of the eye might, with equal probability, be caused by either the gauze or the radium. The testimony of Dr. Nelson concedes that such is true and the evidence on behalf of the defendant is that the gauze had nothing whatever to do with such damage. Under that state of the record the jury was left only to speculate as to that phase of the case. The Supreme Court therefore concluded that the plaintiff was not entitled to the award of $10,000 for loss of the eye and that the trial court was right in eliminating such sum from the judgment. Accordingly the judgment in favor of the plaintiff for $10,000 was affirmed.—*Parker v. Pettit, 138 P. (2d) 592 (Ore., 1943)*

Medical Examinations and Licensure

COMING EXAMINATIONS AND MEETINGS

BOARDS OF MEDICAL EXAMINERS BOARDS OF EXAMINERS IN THE BASIC SCIENCES

Examinations of the boards of medical examiners and boards of examiners in the basic sciences were published in THE JOURNAL, Nov. 30, page 810.

NATIONAL BOARD OF MEDICAL EXAMINERS

NATIONAL BOARD OF MEDICAL EXAMINERS: *Part II.* Dec. 16-17. *Part III.* Boston, Chicago, Jan. 9-11. Sec., Mr. Everett S. Elwood, 225 S. 15th St., Philadelphia 2.

EXAMINING BOARDS IN SPECIALTIES

AMERICAN BOARD OF ANESTHESIOLOGY: *Oral.* Los Angeles, 2d week in April. Sec., Dr. P. M. Wood, 745 Fifth Ave., New York.

AMERICAN BOARD OF INTERNAL MEDICINE: *Written, Oral.* Chicago, Feb. 12-14. Final date for filing application is Jan. 1, 1947. March 17. Asst. Sec., Dr. W. A. Werrell, 1 W. Main St., Madison 3, Wis.

AMERICAN BOARD OF NEUROLOGICAL SURGERY. Examination to be given during the Summer. Applications for examination will be accepted until Feb. 15. Sec., Dr. P. C. Bucy, 912 S. Wood St., Chicago.

AMERICAN BOARD OF OBSTETRICS AND GYNECOLOGY: *Part II.* Pittsburgh. June 1-7. Sec., Dr. Paul Titus, 1015 Highland Bldg., Pittsburgh.

AMERICAN BOARD OF OPHTHALMOLOGY: *Oral. All Groups. Parts I and II.* Dec. 1. Chicago, October 1947. Final date for filing application is March 1. Sec., Dr. S. J. Beach, 56 Ivie Rd., Cape Cottage, Me.

AMERICAN BOARD OF OTOLARYNGOLOGY: *Oral.* St. Louis, Dec. 15 and April 16-19. Sec., Dr. D. M. Lierle, University Hospitals, Iowa City, Ia.

Current Medical Literature

AMERICAN

The Association library lends periodicals to members of the Association and to individual subscribers in continental United States and Canada for a period of three days. Three journals may be borrowed at a time. Periodicals are available from 1936 to date. Requests for issues of earlier date cannot be filled. Requests should be accompanied with stamps to cover postage (6 cents if one and 18 cents if three periodicals are requested). Periodicals published by the American Medical Association are not available for lending but can be supplied on purchase order. Reprints as a rule are the property of authors and can be obtained for permanent possession only from them.

Titles marked with an asterisk (*) are abstracted below.

Alabama State Medical Assn. Journal, Montgomery

16:69-104 (Aug.) 1946

Psychoneuroses and World War II. W. S. Littlejohn.—p. 69.
Development of Army Medical Department: Short Sketch. H. P. Sawyer. —p. 73.
Some Common Urologic Complications Following Abdominal Surgery. J. H. Goode.—p. 85.

16:105-128 (Sept.) 1946

Clinical Importance of Congenital Anomalies of Urinary Tract. E. Burns. —p. 105.
Headaches Associated with Injuries of Cervical Spine: Preliminary Report. S. C. Little.—p. 110.
Pediatric Problems in General Practice. W. A. Daniel Jr.—p. 114.

American Journal of Diseases of Children, Chicago

72:137-250 (Aug.) 1946

Estivoautumnal (Plasmodium Falciparum) Malaria: Survey of 493 Cases of Infection with Plasmodium Falciparum in Children. N. H. Einhorn and W. J. Tomlinson.—p. 137.
*Clinical Ascariasis: Analysis of 202 Cases. J. C. Swartzwelder.—p. 172.
*Human Infections with Salmonella Panama. R. H. High and E. H. Spaulding.—p. 181.
Causes of Prematurity: VIII. Influence of Infections, Chronic Disorders and Accidents on Incidence of Prematurity. Estelle W. Brown, R. A. Lyon and Nina A. Anderson.—p. 189.

Clinical Ascariasis.—Swartzwelder states that of 11,000 stools of clinic and hospitalized patients at the Charity Hospital in New Orleans examined by his associates and himself 426 were found to contain ova of Ascaris lumbricoides. He presents an analysis of the clinical and laboratory data from the case records of 202 persons with clinically evident A. lumbricoides infection admitted to the Charity Hospital of Louisiana during a period of about a decade. The age of 170 patients was under 16 years and of 15 patients over 30. The most common symptoms were abdominal pain or discomfort, passing of ascarids by the anus, the mouth or the nose, vomiting, abdominal or epigastric tenderness, fever, constipation, abdominal distention, cough or cold, nausea, headache and diarrhea. Convulsions, abnormal pulmonary conditions, anorexia, loss of weight, weakness, malaise, restlessness, abdominal rigidity, palpable abdominal masses, dyspepsia and dyspnea ranked next in order of frequency. Abdominal pain was frequently sudden in onset and recurrent in nature. In 18 cases the diagnosis was intestinal obstruction due to A. lumbricoides. In 16 cases the obstruction occurred prior to anthelmintic treatment. In 2 cases the obstruction occurred following treatment with santonin or with carbon tetrachloride. In both cases the termination was fatal. No post-treatment obstruction resulted in any of the cases treated with hexylresorcinol or with oil of chenopodium U. S. P. Six cases of intestinal obstruction were fatal. The most frequent tentative diagnoses included intestinal parasites (helminthiases), ascaris infection, chronic recurrent appendicitis, infection of the upper respiratory tract, gastroenteritis, tuberculosis, intestinal obstruction, subacute appendicitis, epilepsy, intussusception and intestinal intoxication. In over half of the cases in which differential leukocyte counts were done there was an eosinophil count of less than 3 per cent. The maximum eosinophil count was 28 per cent.

Human Infections with Salmonella Panama.—High and Spaulding report 3 cases of human Salmonella panama infections and suggest that S. panama is not primarily an animal pathogen, which is the generally accepted view, but essentially a human parasite. The first of the 3 cases was one of mild gastroenteritis in an adult; the second, one of meningitis successfully treated with sulfadiazine in an infant; the third, one of fatal Salmonella septicemia in a newborn infant. S. panama should be considered as primarily a "human" type of Salmonella the transmission of which is predominantly from man to man rather than from animal to man.

American Journal of Medicine, New York

1:213-314 (Sept.) 1946

*Anticonvulsant Properties of Tridione: Laboratory and Clinical Investigations. L. S. Goodman, J. E. P. Toman and E. A. Swinyard, with technical assistance of Corinne Manuel, M. Merkin and Mary Murata. —p. 213.
*Effects of Total Pancreatectomy in Patient with Diabetes. H. T. Ricketts, A. Brunschwig and Kathryn Knowlton.—p. 229.
Clearance of Inulin, Diodrast, Chloride and Phosphate Under Mercurial Diuresis. Intensive Study of Patient in Severe Cardiac Failure. Edith B. Farnsworth.—p. 246.
Chrysotherapy in Rheumatoid Arthritis: Three Year Study of 142 Cases. C. Ragan and T. L. Tyson.—p. 252.
Diagnosis and Treatment of Diseases of Anorectum. H. E. Bacon, J. P. Fleming, C. H. Smith and others.—p. 257.
Penicillin Aerosol and Negative Pressure in Treatment of Sinusitis. A. L. Barach, B. Garthwaite, C. Rule and others.—p. 268.
Isolation of Virulent Treponema Pallidum from Human Aorta Thirty-Two Hours After Death from Cardiovascular Syphilis. C. K. Hu, Y. Liu, K. C. Chen and C. N. Frazier.—p. 301.

Anticonvulsant Properties of Tridione.—Tridione has been made available as a symptomatic therapy for petit mal epilepsy. Goodman and his associates compared the anticonvulsant properties of tridione in animals with those of diphenylhydantoin and phenobarbital by six different laboratory technics. Of all the results obtained, the antagonism to metrazol is the property which most sharply distinguishes tridione from both diphenylhydantoin and phenobarbital. Of particular significance in relation to the known specificity of tridione against petit mal is its ability to abolish the petit mal-like electroencephalographic dysrhythmia produced in animals by metrazol. On the basis of electroencephalographic and clinical study of a selected group of patients with slow wave dysrhythmias, recommendations have been advanced for the clinical use of tridione alone or in combination with other drugs. A sharp rise in seizure rate may be observed in petit mal patients during the first twenty-four hours of tridione therapy. This transient exacerbation is not a contraindication to the drug and may be followed by complete clinical remission. Although freedom from seizures may continue for weeks after discontinuation of tridione, withdrawal should not be attempted until the patient has been seizure free for many months. Abrupt cessation of tridione medication does not entail the danger of "status epilepticus." Drug treatment for associated grand mal should not be stopped when tridione therapy for petit mal is initiated. If psychomotor electroencephalographic dysrhythmia is associated with a petit mal history, diphenylhydantoin combined with tridione is probably the treatment of choice. An occasional patient may respond well to tridione alone. Preliminary electroencephalographic examination provides a sounder basis than clinical history of seizure type for deciding whether tridione should be used alone or in combination with other agents.

Total Pancreatectomy.—Ricketts and his associates report physiologic and metabolic studies on a man who had undergone pancreatectomy, the completeness of which was established at necropsy. The pancreatectomy was done for carcinoma when the patient was already diabetic and had chronic diarrhea. The stomach, duodenum, spleen and left adrenal also were removed. For approximately three months the patient remained in sufficiently good condition to permit metabolic studies. Loss of the pancreas led to an increase in diarrhea, even though the patient was receiving powdered pancreas in large amounts. Intestinal absorption of both fat and protein, already less than normal before operation, was strikingly diminished thereafter. The large loss of nitrogen in the feces was accompanied with a relatively low urinary loss. Analyses of food and excreta showed a slightly positive calcium and phosphorus balance, despite the severe diarrhea. Extirpation of the pancreas was not followed by any increase in the requirement for insulin, which, with a diet containing 400 Gm. of carbohydrate, averaged about 40 units per day. Sensitivity to insulin was great, the

patient experiencing frequent hypoglycemic reactions. When the patient was maintained on three injections of crystalline insulin per day, the last dose being given before supper, the fasting blood sugars were essentially normal. This is contrary to the usual finding in severe, spontaneous diabetes. Also at variance with the behavior of such patients was the response in the present case to intravenously administered glucose, the resultant blood sugar curves being less "diabetic" than might be expected. The authors think that the considerable loss of nutriment through diarrhea may explain certain apparent differences between the diabetes in this case and the spontaneous disease of ordinary diabetic patients.

American J. Orthodontics and Oral Surgery, St. Louis

32:525-596 (Sept.) 1946

Army Institute of Pathology and Registry of Dental and Oral Pathology. H. A. Swanson.—p. 526.
Evaluation of Biopsy as Diagnostic Aid. J. L. Bernier.—p. 531.
Histogenesis of Cementoma: Report of 15 Cases. J. L. Bernier and H. C. Thompson.—p. 543.
Invasion of Paranasal Sinuses by Tumors of Meningeal Origin. W. W. Hurteau.—p. 556.
Eosinophilic Granuloma of Bone with Primary Oral Manifestations: Report of 3 Cases. M. E. Cox.—p. 569.
*Fibrous Dysplasia (Ossifying Fibroma) of Maxilla and Mandible. H. G. Schlumberger.—p. 579.
Intracranial Epidermoids (Cholesteatomas). W. A. Bennett.—p. 588.

Fibrous Dysplasia of Maxilla and Mandible.—Schlumberger reports 12 cases of fibrous dysplasia (so-called ossifying fibroma) of the maxilla and the mandible in members of the army whose average age was 26 years. Only 1 patient, a 15 year old boy, was a civilian dependent. The maxilla was involved seven times and the mandible four times in the 11 cases of this series in which the bone lesion was solitary. In the single polyostotic case the mandible was the only bone of the skull affected. Curettement or attempted excision of the lesion was the only therapy employed in these cases. Biopsy revealed partially calcified trabeculae of bone arising by direct metaplasia within a connective tissue stroma; these were indistinguishable in their structure and arrangement from fibrous dysplasia occurring in other bones, e. g. the ribs. The arrangement of the new bone in the form of spherules and the presence of nonossified deposits of calcium were frequently observed in these cases but were also found in lesions of the ribs and long bones in cases with a definite diagnosis of fibrous dysplasia reported by other authors. Since microscopic criteria do not exist by which fibrous dysplasia of the maxilla or mandible can be distinguished from so-called ossifying fibroma of these bones and because their clinical behavior is identical, it is concluded that the ossifying fibroma is a variant of monostotic fibrous dysplasia.

American Journal of Psychiatry, New York

103:1-144 (July) 1946

Psychotherapeutic Aspects of Symptomatic Treatment. J. D. Frank.—p. 21.
Role of Conditioned Responses in Emotional Disturbances of War. N. Bromberg.—p. 26.
Rapid Personality Evaluation Based on Minnesota Multiphasic Personality Inventory and Cornell Selectee Index. H. Grant.—p. 33.
Psychosomatic Dermatologic Syndromes in Military Service: Observation of 26 Cases. D. J. Sullivan and E. S. Bereston.—p. 42.
Why 2,276 American Soldiers in Mediterranean Theater of Operation Were Absent Without Leave, Deserted or Misbehaved Before the Enemy. M. P. Manson and H. M. Grayson.—p. 50.
Residuals of Combat Induced Anxiety. C. O. Sturdevant.—p. 55.
On Oriental Stoicism. J. C. Moloney.—p. 60.
Psychologist's Contribution to Psychiatric Hospital. C. O. Cheney and E. I. Strongin.—p. 65.
Physical Signs in Schizophrenia. T. Klingmann.—p. 69.
Cerebral Lesion Resulting in Spatial Disorientation. A. Z. Pfeffer, E. D. Friedman and S. B. Wortis.—p. 72.
Conditioned Response to Fellatio. A. C. Cornsweet and M. F. Hayes.—p. 76.
Selectee and His Complaints. W. Rottersman.—p. 79.
Psychoneurotics in Combat. M. R. Plesset.—p. 87.
Report on Use of Wechsler-Bellevue Scales in Overseas General Hospital. M. I. Teicher and E. Singer.—p. 91.
Autofellatio: Report of Case. M. M. Kessler and G. E. Poucher.—p. 94.
Personal Problems Related to Army Rank. J. D. Frank.—p. 97.
Psychopathic Personality: Rorschach Patterns of 28 Cases. K. D. Heuser.—p. 105.
Veteran Uses General Semantics for Rehabilitation. By the Veteran.—p. 113.

American Journal of Surgery, New York

72:289-496 (Sept.) 1946

Shock of Battle Wounds: Review of Treatment in 2,000 Casualties. R. Birchall.—p. 291.
*Review of Blood Donor Service of American Red Cross. W. Thalhimer and L. H. Tisdall.—p. 300.
Use of Blood and Plasma in Treatment of Battle Casualties. C. P. Emerson Jr.—p. 307.
Penicillin and Its Use in the War Wounded. C. Lyons.—p. 315.
Function of Thoracic Surgery Centers in World War II. D. B. Effler and B. Blades.—p. 319.
Surgical Management of War Wounds of Abdomen. J. M. Snyder.—p. 331.
Perforating Wounds of Colon and Rectum. B. P. Colcock.—p. 343.
Rehabilitation of Injured Hand. S. B. Hardy.—p. 352.
*Bone Surgery of Hand. S. T. Snedecor.—p. 363.
Repair of Avulsion Wounds of Hands and Feet by Flap Graft Technic. L. R. Rubin.—p. 373.
Splints and Casts in Treatment of War Injuries. M. Bosworth.—p. 385.
Fractures of Upper Extremity: Review of Experiences in World War II. W. T. Fitts Jr.—p. 393.
Rehabilitation of Surgical Patient in Army Hospitals in World War II. A. Thorndike.—p. 404.
Fractures and Dislocations of Spine in Warfare. J. T. Daniels.—p. 414.
Acute War Wounds of Spinal Cord: Analysis of 184 Cases. W. G. Haynes.—p. 424.
Management of War Wounds of Cranial Cavity. R. A. Groff.—p. 434.
Penetrating Wounds of Brain: Management in Evacuation Hospital. E. W. Shearburn and E. H. Mulford.—p. 441
Surgical Problems in Late Management of Craniocerebral Injuries, with Special Reference to Repair of Cranial Defects with Tantalum Plate: Analysis of 170 Cases. I. J. Speigel.—p. 448.
Painful Injuries of Nerves and Their Surgical Treatment. J. C. White.—p. 468.
Repair of Peripheral Nerve Lesions. T. I. Hoen.—p. 489.

Blood Donor Service of American Red Cross.—Thalhimer and Tisdall state that donations of 13,326,242 pints of blood were made by approximately 6,660,000 voluntary donors from Feb. 4, 1941 through August 1945. Donors averaged two donations. The American Red Cross Blood Donor Service was inaugurated at the request of the Army and Navy. The National Research Council assumed responsibility for endorsing all technical and scientific procedures and the Red Cross all other responsibilities. An ample supply of plasma was distributed to our forces all over the globe, to all ships, airports, hospitals and even to front lines and invasion beaches. Methods were developed for fractionating plasma, which proved useful for many purposes. When it was recognized that adequate treatment of hemorrhage and shock due to hemorrhage required immediate transfusion of whole blood, a project for the procurement of whole blood in the continental United States and its shipment to the various combat zones was jointly undertaken by the Army and Navy in cooperation with the Red Cross Blood Donor Service. On the basis of official reports, eye witness accounts and the related experiences of hundreds of army and navy physicians, it may be stated that the results of the use of whole blood shipped from the United States were most beneficial and that the reaction rate at least approximated the rates prevailing in the best civilian hospitals in this country. Some 380,000 pints of whole blood was procured, processed and shipped, with excellent results.

Bone Surgery of Hand.—Snedecor presents various types of bone surgery which have accomplished an improvement of function in severely deranged hands. Bone grafts have been used to form a first metacarpal, to make a bone block between the first and second metacarpals, and in many varied forms to make up loss of bone substance in metacarpals. A metatarsal head with its cartilaginous covering was successfully transplanted onto a metacarpal shaft to form a new metacarpophalangeal joint. Malunion of metacarpals often required correction by osteotomies to realine the metacarpal heads and restore the intrinsic muscle function. Rotation osteotomies were also useful to correct malunion of both metacarpals and the phalanges. Closing in of the hand by metacarpal shifts onto the bases of their vacant neighbors was discovered to be an advantageous procedure under proper indications. Simple arthroplasties of the metacarpophalangeal joints were practical and reasonably successful. Failures of union have been observed almost not at all either after osteotomies or after bone grafts.

Am. J. Syphilis, Gonorrhea and Ven. Dis., St. Louis

30:405-512 (Sept.) 1946

Penicillin in Treatment of Neurosyphilis: I. Asymptomatic Neurosyphilis. J. E. Moore and C. F. Mohr.—p. 405.
Systemic Treatment of 227 Cases of Arsenic Poisoning (Encephalitis, Dermatitis, Blood Dyscrasias, Jaundice, Fever) with 2,3-Dimercaptopropanol (BAL). H. Eagle and H. J. Magnuson.—p. 420.
Studies on Biologic Relationship Between Causative Agents of Syphilis, Yaws and Venereal Spirochetosis of Rabbits: I. Observations on Treponema Cuniculi Infection in Rabbits. Charlotte McLeod and T. B. Turner.—p. 442.
Id.: II. Comparison of Experimental Disease Produced in Rabbits. Charlotte McLeod and T. B. Turner.—p. 455.
*Syphilitic Nephrosis as Manifestation of Renal Herxheimer Reaction Following Penicillin Therapy for Early Syphilis: Case Report. V. Scott and E. G. Clark.—p. 463.
Therapeutic Effectiveness of Relatively Crude Commercial Penicillin in Early and Late Rabbit Syphilis. W. L. Fleming and Mary H. Wolf.—p. 468.
Rapid Treatment of Early Syphilis with Combined Use of Penicillin and Mapharsen. H. N. Bundesen, R. M. Craig, G. X. Schwemlein, R. L. Barton and T. J. Bauer.—p. 475.
Penicillin by Mouth in Treatment of Late Cutaneous Syphilis: Report of Case. Evelyn Wallace and W. D. Paul.—p. 480.
Oral Penicillin Treatment of Gonorrhea. A. Cohn, B. A. Kornblith and I. Grunstein.—p. 485.
Value of Quantitatively Standardized Complement Fixation Test in Diagnosis and Treatment of Early Syphilis. E. R. Maillard and Anne Orzel.—p. 490.
Surgical Treatment of Inguinal Lymphogranuloma Venereum: Analysis of 613 Cases in Male. H. A. Tucker.—p. 495.

Nephrosis Following Penicillin Therapy of Syphilis.—Scott and Clark report a case of secondary syphilis in a man aged 31 in which the classic nephrotic syndrome developed and which spontaneously and rapidly subsided without further antisyphilitic treatment following penicillin therapy. Treatment had been accompanied with a severe febrile Herxheimer reaction. This case demonstrates that subclinical involvement of the kidney may exist in early syphilis and that a focal Herxheimer reaction affecting a subclinically involved renal parenchyma may produce the nephrotic syndrome (syphilitic nephrosis).

Annals of Surgery, Philadelphia

124:161-478 (Aug.) 1946. **Partial Index**

Experience with Curare in Anesthesia. Virginia Apgar.—p. 161.
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Acute Intussusception in Infants and Children. B. M. Hogg and E. J. Donovan.—p. 262.
*Prevention of Wound Infection by Injection of Nontoxic Antibacterial Substances. E. I. Howes.—p. 268.
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Report on Trench Foot and Cold Injuries in European Theater of Operations. O. C. Leigh.—p. 301.
*Importance of Whole Blood Transfusions in Management of Severe Burns. J. J. McDonald, E. F. Cadman and J. Scudder.—p. 332.

Thiouracil Thyrotoxicosis.—Aranow and his associates review observations on thiouracil treatment of 77 cases of primary toxic goiter, 30 cases of recurrent toxic goiter and 47 cases in which thyroidectomy was done. They found that the incidence of "permanent" remissions obtained in primary thyrotoxicosis by the use of thiouracil is so small that they do not advocate it as the sole therapeutic agent. Prolonged treatment with thiouracil in primary thyrotoxicosis should probably be reserved for the categories of cases in which (1) operation has been refused, has been ineffective or is inadvisable, (2) malignant exophthalmos is feared, (3) the adolescent age group is involved or (4) roentgenotherapy has been administered without benefit and operation is not feasible. As a preparation for operation the use of iodine alone is advocated for the average case of toxic goiter because of the present incidence of toxic reactions with thiouracil and the length of time required for preparation with this drug. Thiouracil can be used to advantage as preparation for operation in the poor risk cases such as the thyrocardiac or those in which thyrotoxicosis is extreme and iodine is not tolerated or prolonged preoperative treatment is required. Thiouracil therapy is promising in a selected group of cases with recurrence of symptoms after operation. The permanent remissions in thiouracil treatment of recurrent toxic goiter are few but the drug does offer a means of control of hyperactivity over long periods.

Prevention of Wound Infection by Antibacterial Substances.—Howes says that a mixture of 200 units of streptomycin per cubic centimeter and 5 per cent of sulfamylon (4-amino-2-methyl benzene sulfonamide hydrochloride) was demonstrated as being capable of killing a three hour growth of bacteria on a blood agar plate. This combination of streptomycin and sulfamylon was demonstrated to be innocuous to tissues. It was suggested that the mixture of streptomycin and sulfamylon should be an ideal subcutaneous antiseptic. It was used in 30 clinical cases without untoward effects and without infection. The author made studies on animals. A defect 3 cm. square was cut in the skin of the back of the rabbit just lateral to the spinal column. The loose subcutaneous tissue and fascia were excised and the underlying muscle was vigorously crushed with a Kocher clamp. The wound was then contaminated with bacteria, either floor dirt or a twenty-four hour growth of a specific bacterium being used. The wound was then treated with the combination of streptomycin and sulfamylon. Infection was prevented when treatment was carried out immediately after infliction and contamination of the wound, but it failed to prevent infection in wounds treated three hours after infliction and contamination. The inclusion of the bacteria within leukocytes is offered as a possible explanation for the protection of the bacteria against the action of the antibacterials after three hours. Failing to penetrate to the bacteria within the leukocyte, the cell may subsequently die and liberate them unharmed to recontaminate the wound. Repeated injections and washing of the wound with an established localized infection did not hasten resolution of the suppuration. The author stresses that, if this combination of antibacterial substances is used clinically to prevent infection in wounds, the principles of good surgery should not be neglected. Use should be limited to contaminated wounds relatively free of traumatized tissue and foreign bodies. Other antibacterials can be substituted for the sulfamylon and streptomycin if they kill bacteria quickly in the presence of blood, have a wide range of activity, do not destroy or irritate tissue at the bactericidal concentration and are nontoxic.

Whole Blood Transfusions in Burns.—The 10 patients selected for the present analysis by McDonald and his associates suffered flame burns of from 30 to 80 per cent of their body surfaces and were treated under the direction of various members of the surgical staff of the Presbyterian Hospital, New York. The first 4 patients had overwhelming burns and appeared to have little or no hope of survival but are presented as a comparison of four types of shock therapy. Of the remaining 6 patients 2 died in the postshock phase and 4 survived. The authors conclude that replacement therapy in burn shock should be directed toward the restoration of all deficits in the circulating blood. Whole blood transfusions fulfil these requirements more nearly than any other single agent. Water and electrolytes can be administered to better advantage by mouth than by vein and will be absorbed in adequate amounts provided transfusions also are given. Sodium chloride solution in combination with lactate or bicarbonate is a more rational electrolyte mixture than sodium lactate solution alone in view of the tendency to alkalosis and hypochloremia which may result from vomiting and overalkalization in burn shock. The relative losses in plasma proteins and red cell mass may vary widely and are difficult to estimate during the period of hemoconcentration. In general, plasma losses will predominate in extensive second degree burns, while in third degree burns the red cell mass lost from the circulation may equal or even exceed the losses in plasma volume. During the healing phase of a severe

burn whole blood should be administered in amounts adequate to overcorrect the anemia. If this is done the problem of maintaining nitrogen balance will be simplified. In the presence of anemia and hypoproteinemia uncontrolled electrocyte therapy by mouth or by vein is contraindicated since it will increase cellular edema and may lead to fatal pulmonary edema.

Archives of Dermatology and Syphilology, Chicago

54:255-376 (Sept.) 1946

Use of Penicillin in Treatment of Syphilis in Pregnancy. H. N. Cole, S. Ayres, J. H. Barr and others.—p. 255.
Chromoblastomycosis: Report of 2 New Cases Observed in Isthmus of Panama. C. Calero.—p. 265.
Rat Mite Dermatitis: Ascariasis Caused by Tropical Rat Mite, Liponyssus Bacoti Hirst. M. E. Lowell.—p. 278.
Urinary Excretion of Porphyrin in Dermatoses. I. Zeligman.—p. 281.
*Allergic Dermatoses Complicating Penicillin Therapy. G. H. Bauer.—p. 292.
In Vitro Fungistasis by Bacterium (Bacillus Subtilis Var. XG and XY). G. M. Lewis, Mary E. Hopper and Selma Shultz.—p. 300.
Relation of Quinacrine Hydrochloride to Lichenoid Dermatitis (Atypical Lichen Planus). J. M. Bazemore, H. H. Johnson, E. R. Swanson and J. M. Hayman.—p. 308.
Complications of Lichenoid Dermatitis: Glomerulonephritis and Severe Pigmentary Changes in Exfoliative Stage of Lichenoid Dermatitis.—p. 325.
Exfoliative Dermatitis Due to Polyvalent Arsenical Sensitivity: Report of Case. L. J. Underwood.—p. 330.
Cutaneous Leishmaniasis (Oriental Sore): Report of Autochthonous Cases Observed in Haifa. S. Gill.—p. 333.
Dermatitis Due to Quinacrine Hydrochloride. F. T. Becker.—p. 338.

Allergic Dermatoses Complicating Penicillin Therapy.—According to Bauer, the reactions to penicillin are usually of an allergic nature and are then manifested clinically as some type of dermatitis. There are three clinical types of reaction to penicillin: (1) urticaria, (2) the erythematovesicular group of reactions and (3) contact dermatitis. The first two follow only the injection route, while contact dermatitis occurs only after external exposure. Although the exact allergen could not be identified in the 2 cases of contact dermatitis resulting from commercial penicillin sodium, studies indicated that neither crystalline penicillin sodium G nor the penicillin culture medium was responsible. An analysis of cases of the erythematovesicular type of reaction and the results of tests indicate that the mechanisms behind this erythematovesicular reaction and the dermatophytids are similar and may possibly be identical. The diagnostic value of intradermal tests in this group will be greatly increased if they are made in the dermatitic area rather than on the forearms. Cutaneous tests are of only limited value in the diagnosis of the three types of dermatitis discussed in this report. Identification of the exact allergens in these dermatoses must wait until more refined commercial preparations are developed and until the purified penicillin fractions become available for testing.

Archives of Internal Medicine, Chicago

78:125-254 (Aug.) 1946

*Coronary Arteriosclerosis, Coronary Anastomoses and Myocardial Infarction: Clinicopathologic Study Based on Injection Method. A. Ravin and E. F. Geever.—p. 125.
*Fulminating Meningococcic Septicemia Associated with Adrenal Lesions: Analysis and Discussion of 7 Cases. J. M. Kinsman, C. A. D'Alonzo and S. Russi.—p. 139.
Rheumatic Fever in Naval Enlisted Personnel: II. Effectiveness of Intensive Salicylate Therapy in Cases of Acute Infection. R. C. Manchester.—p. 170.
Changes in Hemoglobin and Total Plasma Protein After Injection of Mercurophylline. A. De Vries.—p. 181.
Congenital Dilatation of Pulmonary Arterial Tree: Relation to Ayerza's Disease and Primary Pulmonary Arteriosclerosis. M. M. A. Gold.—p. 197.
Gastroenterology: Review of Literature from July 1944 to June 1945. W. L. Palmer, W. E. Ricketts and S. N. Maimon.—p. 210.

Changes in Coronary Arteries.—According to Ravin and Geever, Schlesinger's method for postmortem study of changes in the coronary arteries has opened a new field in the study of disease of these arteries. The authors examined a series of 166 hearts. In many cases the heart was normal, the cause of death being unrelated to it. The coronary arteries were occluded in 18 hearts. Seven specimens revealed more than one occluded vessel. Thirty-six hearts showed interarterial anastomoses. Anastomoses without occlusion were observed in 21 hearts. Occlusion with infarction occurred in 13 hearts. Occlusion without infarction was encountered in 5 hearts. Infarction without occlusion of the coronary arteries was found in 2 hearts. Some hearts showed uniformly hypoplastic arterial systems. The hypoplasia was considered a factor in the death of 1 patient with arteriosclerosis, thrombosis and subsequent myocardial fibrosis. In 11 patients over 80 years of age 9 hearts showed mild to moderate arteriosclerosis and scattered myocardial fibrosis. The other 2 showed advanced arteriosclerosis, anastomoses, occlusion and infarction. Anomalies of the coronary arteries involved mainly the left circumflex vessel. In 1 case the right coronary artery was absent. There is an important relation between the development of anastomoses and the prognosis and treatment of coronary arteriosclerosis and occlusion.

Meningococcic Septicemia.—Kinsman and his associates report 7 cases of proved fulminating meningococcic septicemia, with recovery in 2. In the beginning the illness was usually diagnosed as an ordinary infection of the respiratory tract. An eruption developed within three to twenty-four hours after the onset. Signs of shock appeared in twelve to twenty-four hours. Symptoms suggesting meningitis were usually present: Five of the 7 patients had pleocytosis; cultures of the spinal fluid of the same 5 patients yielded meningococci. Cultures of the blood of 5 patients were positive for meningococci. Albuminuria and azotemia were the rule. In 3 of the fatal cases adrenal hemorrhage was shown, while in the other 2 there were adrenal changes consisting of zonal degeneration and conspicuous congestion in the inner layers of the cortex, with "tubular changes" in the outer layer. In 1 case there were myocardial changes. It is believed that the cause of the circulatory collapse is the effect of the bacterial poisons on all the tissues of the body. The adrenal glands play only a part. A depletion of vitamin C may be a factor. The theory is advanced that the increased demand on the adrenal glands, as a result of the infection, depletes the cortical cells of their lipoid (hormone-containing) material; the cells degenerate more rapidly than normally, producing the "tubular" pattern in the outer layers and more conspicuous lesions in the inner layers, with eventual lysis of many of the cells before they have reached their usual site of death; this stage is considered reversible. Later, as a result of the loss of support of the sinusoids because of the premature death of the cortical cells, rupture and hemorrhage may occur—an irreversible stage. The patient may die before hemorrhage occurs. The primary aim of treatment is to overcome the infection. In addition to the supportive measures usually advocated, it is suggested that ascorbic acid might be of benefit.

Archives of Neurology and Psychiatry, Chicago

56:245-364 (Sept.) 1946

*Pretraumatic Personality and Psychiatric Sequelae of Head Injury: II. Correlation of Multiple, Specific Factors in Pretraumatic Personality and Psychiatric Reaction to Head Injury, Based on Analysis of 101 Cases. H. L. Kozol.—p. 245.
Effects of Denervation on Fasciculations in Human Muscle: Relation of Fibrillations. F. M. Forster, W. J. Borkowski and B. J. Alpers.—p. 276.
Toxicity of Quinacrine (Atabrine) for Central Nervous System: III. Experimental Study on Human Subjects. T. Lidz and R. L. Kahn.—p. 284.
Ring Scotoma and Tubular Fields: Their Significance in Cases of Head Injury. M. B. Bender and H. L. Teuber.—p. 300.

Sequelae of Head Injury.—Kozol subjected 101 patients with acute head injuries to intensive study of multiple factors in the pretraumatic and the posttraumatic personality status. In a number of patients neurotic symptoms appeared for the first time after head injury. Psychologic changes were most noticeable shortly after discharge from the hospital and were at a maximum three to six weeks after discharge. In general they were receding at the end of three months. Approximately 50 per cent of the patients showed some persistence of symptoms at six months, and approximately 15 per cent had symptoms which persisted a year or longer. The duration of incapacity for work paralleled the persistence of psychologic symptoms. Patients with pretraumatic psychoneurotic personalities showed a greater proportion of posttraumatic psychiatric symptoms than did patients in other groups. There was no close correlation

between the severity of the acute injury of the brain and the severity of the sequelae. There was high correlation between the existence of persistent complicating psychosocial factors, such as continuing compensation, pending litigation, occupational stresses and persistent associated bodily injuries, and the severity and persistence of psychiatric sequelae. The psychiatric sequelae were usually the resultant of various factors.

Bulletin of Johns Hopkins Hospital, Baltimore

79:97-206 (Aug.) 1946

Transmission of Primary Atypical Pneumonia to Human Volunteers: I. Experimental Methods. Commission on Acute Respiratory Diseases. —p. 97.
Effect of Method of Administration on Therapeutic Efficacy of Sodium Penicillin in Experimental Syphilis. H. Eagle, H. J. Magnuson and R. Fleischman.—p. 168.
Perfectionism in Medicine. R. Cole.—p. 190.

Bull. of the U. S. Army Med. Dept., Washington, D. C.

6:203-346 (Sept.) 1946

*Healing Time in Peptic Ulcer. G. M. Cummins Jr., M. I. Grossman and A. C. Ivy.—p. 288.
Adenomatosis versus Pseudopolyposis of Large Bowel. S. Z. Hawkes and R. K. Shields.—p. 302.
Diagrammatic Representation of Rh Blood Types. A. S. Wiener. —p. 311.
Army Hospital Ship. J. A. Goodhart.—p. 321.
Psychiatric and Tactical Situations in Armored Division. E. W. Mericle.—p. 325.
Bacteriologic Laboratory in Combat Area. M. Michael Jr.—p. 335.

Healing Time in Peptic Ulcer.—Cummins and his associates found that accurate data are not available on the rate of healing of gastric ulcers, although the healing time of peptic ulcers is important in evaluating new methods of treatment and judging the efficacy of treatment in individual cases. In the 69 cases reviewed, fluoroscopic study and serial roentgenograms were taken on all original and subsequent examinations. All patients were subjected to the same therapeutic regimen. One teaspoon of a mixture of sodium bicarbonate and calcium carbonate in the proportion of 1 to 3 in water was given every two hours from 8 a. m. to 8 p. m. and at night if awakened by distress. The administration of alkalis was continued on this schedule for twenty-eight days; after that time they were given thirty minutes after meals, before retiring and on awakening at night. Half-and-half mixture of milk and cream 6 ounces every two hours from 7 a. m. to 9 p. m. was given for the first twenty-eight days of the regimen, following which the mixture was given between meals and in the evening. Food by mouth was begun on the fourth day by the gradual addition of farina, poached or boiled eggs, toast, puréed vegetables and ground, boiled or broiled beef. The healing time was judged by the time of disappearance of the crater radiologically. The average healing time for duodenal ulcers was thirty-seven days and for gastric ulcers was forty-two days. No correlation was found between the healing time and the size of the crater, age, recurrence or duration of symptoms.

Canadian Medical Association Journal, Montreal

55:199-326 (Sept.) 1946

Early Recognition of Uterine Cancer. W. G. Cosbie.—p. 237.
Observations on Surgical Relief of Pain in Cancer. F. Turnbull.—p. 241.
*Penicillin in Pyoderma. N. M. Wrong.—p. 244.
*Paraplegia Following War. E. H. Botterell, A. T. Jousse, C. Aberhart and J. W. Cluff.—p. 249.
Pruritus Ani. C. M. Gardner.—p. 259.
Ureteritis Cystica and Some Renal Anomalies. H. Ostry.—p. 262.
Nasal Mechanisms: Their Maintenance and Repair. A. W. Proetz. —p. 264.
Pelvic Pain. K. T. MacFarlane.—p. 267.
Chronic or Recurrent Diarrhea. M. Baird.—p. 273.
Amebiasis. J. P. Fletcher, A. A. Dougan and G. K. Sammon.—p. 278.
Significance of Sedimentation Rate to General Practitioner. A. A. Numbers.—p. 284.

Penicillin in Pyoderma.—Wrong has used penicillin extensively in the treatment of pyogenic skin infections for over two years. Bacteriologic studies are important in any investigation of the effect of penicillin in pyoderma. Staphylococcus pyogenes occurs in 90 per cent or more of all skin infections, and the percentage of its penicillin resistant strains is between 5 and 10. Penicillin has proved effective in the treatment of uncomplicated impetigo, ecthyma (the ointment being the method of choice) and erysipelas. Initial results may be good, but relapses are common, with sycosis of the beard, folliculitis, impetigo complicated by an underlying seborrheic dermatitis, otitis externa or sulfonamide dermatitis, and with furunculosis. Penicillin is of little or no value in common acne, rosacea and pyoderma caused by penicillin resistant organisms. The chief complications of penicillin therapy are dermatitis and urticaria. Dermatitis may develop in a few hours, a few days or even a few weeks after application of penicillin to the skin. The dermatitis subsides fairly rapidly with cold boric acid compresses. Benadryl appears to be of real value in controlling urticaria which follows administration of penicillin. The incidence of both complications seems to be increasing. The efficacy of this antibiotic is seriously affected by the complications.

Paraplegia Following War.—Botterell and his associates observed 103 posttraumatic paraplegic patients with stable spinal cord who were returned from overseas and were treated in Toronto at a center fully equipped and specially staffed to deal with all aspects of treatment and retraining during the period of February 1945 to June 1946. Forty-nine patients presented complete injuries of the spinal cord, while 54 had incomplete injuries, particularly in the lumbar and sacral regions. Death occurred in 7 instances and was considered to be due primarily to disturbances of nutrition, with genitourinary sepsis as a contributory factor. The treatment of the paralyzed bladder in these 103 patients, while overseas, consisted in suprapubic cystotomies in 77 and urethral drainage in 17; 9 had but transient retention requiring catheterization on a few occasions. At the center in Canada, tidal drainage remains the treatment of choice. Of the 77 cystotomies 61 have been closed, 24 by operation and 37 healed following institution of urethral drainage by a retention urethral catheter. In patients in whom infection with gram-negative urea splitting organisms was rife, administration of streptomycin was of substantial value and was continued until the suprapubic wound was healed and the urethral catheter removed. Anterior rhizotomy has been performed on 5 patients in whom the mass flexion reflex was disabling, and all have improved substantially. In 16 of 20 patients sacral, trochanteric and ischial pressure sores have been successfully closed with full thickness skin by rotation flaps. Bilateral pain tract section has proved of great value in the treatment of 4 patients with disabling pain who had lesions involving the cauda equina. Retraining commences while the patient is still in bed and gradually progresses. By grasping a bed frame exerciser the patient may be enabled to turn himself independently at two hour intervals by day and by night. Long leg braces of chrome molybdenum have been evolved and are put forward as being particularly suitable for paraplegic patients. Custom made boots of modified hockey cut type, light in weight and particularly flexible, are recommended as a means of preventing pressure sores of the feet.

Cincinnati Journal of Medicine

27:595-674 (Sept.) 1946

Paraplegia Following War. E. H. Botterell, A. T. Jousse, C. Aberhart and J. W. Cluff.—p. 595.
*Relationship of Smoke to Pneumonia and Other Infections of Respiratory System. C. A. Mills.—p. 624.
Steam Locomotive and Atmospheric Pollution. C. A. Mills.—p. 634.

Relationship of Smoke to Pneumonia and Other Respiratory Infections.—Mills points out that certain industrial cities, as a result of their local topographical features, present sharp local differences in the degree of pollution. Cincinnati and Pittsburgh are two such cities. The sootfall in both cities is highest in the low lying areas of the river bottoms. The author cites figures which indicate the close relationship of high pneumonia death rates to heaviest sootfall. Atmospheric pollution with coal combustion products sharply increases the respiratory disease hazards of the inhabitants of an industrial city. Present day pneumonia and tuberculosis statistics in Pittsburgh and Cincinnati, showing death rates which rise sharply with increasing degrees of atmospheric pollution, provide emphatic support for the Ruhr basin findings of Ascher many years ago. Morton, in studying a large series of surgical records, found postoperative pneumonia to be six times more prevalent among patients who had been tobacco smokers up to

the time of hospitalization than among nonsmokers. The author concludes that there exists a direct and highly significant relationship between air pollution and infectious diseases of the respiratory tract in man.

Delaware State Medical Journal, Wilmington

18:167-194 (Aug.) 1946

Treatment of Poliomyelitis Under Orthodox, Kenny and Prostigmine Methods. G. J. Boines.—p. 167.
Evaluation of Spinal Fluid Examination in Patients with Poliomyelitis. G. J. Boines and O. J. Pollak.—p. 171.
Interpretation of Semen Studies. O. J. Pollak.—p. 175.
Urologic Observations in European Theater of Operations. N. L. Cannon. —p. 179.
Fetal Blackout. I. Slovin.—p. 183.
Dissecting Aneurysm of Right Colic Artery. O. J. Pollak.—p. 186.

Endocrinology, Springfield, Ill.

39:85-160 (Aug.) 1946

Inhibitors of Hyaluronidase in Blood Serums and Their Effect on Follicle Cell Dispersal. S. L. Leonard and R. Kurzrok.—p. 85.
Effect of Purified Gonadotropes on Androgen-Secreting Ability of Testes of Hypophysectomized Cocks. A. V. Nalbandov, R. K. Meyer and W. H. McShan.—p. 91.
Experimental Production of Menstrual Anomalies. Doris H. Phelps. —p. 105.
Weanling Guinea Pig as Test Object for Estrogen Assays. C. G. Hartman, J. L. Littrell and J. Tom.—p. 120.
Excretion of Urinary Corticoids and 17-Ketosteroids in Normal Individual. Eleanor H. Venning and V. Kazmin.—p. 131.
Disturbance in Iodine Metabolism Produced by Thiocyanate: Mechanism of Its Goitrogenic Action with Radioactive Iodine as Indicator. J. Wolff, I. L. Chaikoff, A. Taurog and L. Rubin.—p. 140.
Influence of Ingested Estrogens on Feed Intake, Metabolic Rate and Lipemia in Male Fowl. S. Bird.—p. 149.

Gastroenterology, Baltimore

7:153-284 (Aug.) 1946

Military Gastroenterology—The Summing Up. D. T. Chamberlin. —p. 162.
*Differential Diagnosis of 207 Hospitalized Cases of Peptic Ulcer. R. C. Kirk.—p. 168.
Correlated Gastroscopic and Psychiatric Studies of Soldiers with Chronic Nonulcerative Dyspepsia. J. A. Halstead, I. R. Schwartz, S. R. Rosen and others—p. 177.
Clinical Findings in American Soldiers Released From German Prison Camp. M. Kraemer.—p. 191.
Gastrointestinal Bleeding in Hereditary Hemorrhagic Telangiectasia: Historical Review and Case Report with Gastroscopic Findings and Rutin Therapy. S. D. Kushlan.—p. 199.
Effects of Beta-Dimethylaminoethyl Benzilate Hydrochloride on Intestinal Activity. K. G. Wakim, C. E. Powell and K. K. Chen.—p. 213.
Effect of Glucose on Motility of Stomach and Small Intestine. E. J. Van Liere, D. W. Northup and J. C. Stickney.—p. 218.
Effect of Pilocarpine on Mucous Secretion by Pyloric Mucosa. J. S. Ivy.—p. 224.

Differential Diagnosis of Peptic Ulcer.—Kirk presents a study that was made at the Station Hospital, Fort Sill, Oklahoma. In a sixteen month period 1,306 enlisted men were admitted to the gastrointestinal section. During this period 207 soldiers were proved to have peptic ulcer. There were 200 with duodenal ulcer and 7 with gastric ulcer, a ratio of 28:1. This report is concerned chiefly with the 200 cases of duodenal ulcer. Midepigastric pain occurring late at night and radiating into the mid back appears diagnostic of active duodenal ulcer. No correlation has been obtained between the gastric analysis and the severity of the ulcer or of the complaints. Free hydrochloric acid was absent in the fasting contents of the stomach in 26 cases and in the test meal contents in 12 cases. An increase in the total count and the percentage of polymorphonuclear cells is strong evidence of a penetrating ulcer. A duodenal ulcer has a 10 per cent chance of producing serious bleeding and a 5 per cent chance of perforating during its course. Alcohol and tobacco are not implicated as etiologic factors in this disease. The x-ray proof of ulcer was present in 100 per cent of this series. Comparing these 200 ulcer patients with 200 others in whom peptic ulcer had been suspected but could not be proved, it was found that the peptic ulcer patients as a whole showed no greater or lesser degree of psychiatric imbalance than patients with organic heart disease, tuberculosis or diabetes; that is, the emotional concept of the genesis of duodenal ulcer could not be proved.

Illinois Medical Journal, Chicago

90:73-144 (Aug.) 1946

Gallbladder and Duct Problem. R. L. Sanders.—p. 111.
Corrective Surgery of External Nasal Pyramid and Nasal Septum for Restoration of Normal Physiology: I. Introduction to Individual Procedures for Surgery of External Nasal Pyramid: II. Surgery of Anterior and Posterior Portions of Nasal Septum: III. Surgery of External Nasal Pyramid Combined with Surgery of Nasal Septum. M. H. Cottle and R. M. Loring.—p. 119.
Antituberculosis Vaccination. I. S. Neiman.—p. 131.
Carcinoma of Male Breast: Report of Case. A. C. Webb and R. C. Stepto.—p. 135.

Journal of Aviation Medicine, St. Paul

17:279-392 (Aug.) 1946

Future of Research in Aviation Medicine. A. C. Ivy.—p. 280.
Studies on Positive Pressure Respiration: I. General Aspects and Types of Pressure Breathing; II. Effects on Respiration and Circulation at Sea Level. A. L. Barach, M. Eckman, E. Ginsburg and others. —p. 290.
Civilian Aviation and Medical Education. R. W. Keeton.—p. 321.
Studies on Altitude Decompression Sickness: I. Symptomatology. J. S. Gray, S. C. F. Mahady, R. L. Masland and H. S. Wigodsky.—p. 333.
Effectiveness of Some Motion Sickness Remedies in Preventing Air Sickness in Air Force Navigation Students. P. K. Smith.—p. 343.
Use of Hyoscine Hydrobromide for Prevention of Airsickness in Flexible Gunnery Students. P. K. Smith.—p. 346.
Device for Demonstrating Effects of Anoxia on Vision. A. Chapanis. —p. 348.
Effect of Pressure Breathing on Circulation at High Altitude as Measured by Ballistocardiograph. N. Molomut and S. C. Allen.—p. 357.
Automatic Rip Cord for High Altitude Bail Out. W. Siri and C. A. Tobias.—p. 364.

Journal of Clin. Endocrinology, Springfield, Ill.

6:535-594 (Aug.) 1946

Clinical Method for Chromatographic-Colorimetric Determination of Urinary 17-Ketosteroids. I. Elisabeth Dingemanse, Leonora G. Huis in't Veld and B. M. DeLaat.—p. 535.
*Testosterone Propionate Therapy in 100 Cases of Angina Pectoris. M. A. Lesser.—p. 549.
Addison's Disease in Infant. J. C. Jaudon.—p. 558.
Metabolic Studies in Children Fed Milk from Cows Receiving Synthetic Thyroprotein. M. Bruger and Flora F. Silberbush.—p. 565.
Therapeutic Use of Testosterone in Aqueous Suspension. S. C. Freed. —p. 571.
Hereditary Exophthalmic Goiter—Report of 11 Cases in One Family. N. F. Boas and W. B. Ober.—p. 575.

Testosterone Propionate in Angina Pectoris.—Lesser treated angina pectoris in 92 men and 8 women with testosterone propionate. Twenty-five mg. of the hormone was administered twice a week for the first two weeks, followed by weekly 25 mg. injections, with an average of twelve injections in the whole series. No untoward effects were observed. Ninety-one of the patients improved for periods of from two to thirty-four months. No appreciable improvement was observed following control injections of plain sesame oil, although the same patients responded when placed on testosterone propionate therapy. Four patients were studied by exercise tolerance tests before and during the course of treatment. In each of these patients the amount of exercise which could be tolerated before the development of an anginal attack was vastly increased under testosterone therapy, and the severity of attacks, as measured by the duration of the pain, was correspondingly diminished. In each case subjective improvement was reported before objective changes could be demonstrated by the test employed.

Journal of Investigative Dermatology, Baltimore

7:153-208 (Aug.) 1946

Tropical Anhidrotic Asthenia (Thermogenic Anhidrosis) and Its Relationship to Prickly Heat. M. B. Sulzberger, H. M. Zimmerman and K. Emerson.—p. 153.
Cytology of Molluscum Contagiosum, with Special Regard to Significance of So-Called "Vacuoles." E. Meirowsky, S. Keys and G. Behr. —p. 165.
Some Newer Bases for Use in Cutaneous Therapy. J. G. Hopkins. —p. 171.
Treatment of Pyodermas with Interface Active Solution of Tyrothricin. G. M. MacKee, Marion B. Sulzberger, Franz Herrmann and Florentine L. Karp.—p. 175.
Biologic Assay of Poison Ivy Extract. J. E. Dunn and Barbara S. Smith.—p. 185.
Preliminary and Short Reports: Effect of Pyribenzamine on Dermographism (Urticaria Factitia). R. L. Baer and M. B. Sulzberger.—p. 201.
Action of Clavacin on Some Dermatophytes: Preliminary Report. J. A. Tolmach and K. Loewenthal.—p. 207.

Journal of Nervous and Mental Disease, New York

104:237-350 (Sept.) 1946

Paroxysmal Slow Waves in Electroencephalograms of Patients with Epilepsy and with Subcortical Lesions. Margaret Lennox and B. S. Brody.—p. 237.
Lückenschädel in Patient with Amnesia Amenable to Hypnotherapy: Personality Study. J. M. Schneck.—p. 249.
*Preliminary Report on Effect of Glutamic Acid Administration in Mentally Retarded Subjects. Kathryn Albert, P. Hoch and H. Waelsch. —p. 263.
Classification of Types of Behavior Noted in General Prisoners. E. H. Malone.—p. 275.
Problems of Military Neuropsychiatry. S. Burack.—p. 284.
Electroshock and Personality Structure. E. P. Mosse.—p. 296.
Concept of Induced Insanity in Family Units. F. J. Kallmann and Jean S. Mickey.—p. 303.

Effect of Glutamic Acid on Mentally Retarded Subjects.—Albert and her associates administered glutamic acid to 8 persons with mental deficiency whose chronologic age ranged from 6 to 26 years and the mental age from 2 to 8 years. The I. Q. varied between 22 and 73. After the I. Q. level was established, the patients were given placebos or glutamic acid. An average of eighteen tablets a day of 0.5 Gm. each were given. A significant rise of mental age was found during the administration of the amino acid. During the successive placebo period the patients' I. Q. dropped back to the level maintained before glutamic acid was given. The authors do not wish to imply that cases of secondary mental deficiency and other forms of feeblemindedness may be cured with glutamic acid; but there is some indication that a limited influence can be demonstrated en some of these patients. Mental defects have been considered unalterable, and treatment has been concentrated on the social and educational aspects. The authors felt that attempts should be made to test the possibility of improving brain function by biochemical means. The results obtained with glutamic acid are considered to be a starting point for further investigations.

Journal of Neurophysiology, Springfield, Ill.

9:349-418 (Sept.) 1946

Presence and Action of Acetylcholine in Experimental Brain Trauma. M. B. Bornstein.—p. 349.
Relation of Electric Potential Changes to Contracture in Skeletal Muscle. S. W. Kuffler.—p. 367.
Righting and Other Postural Activity in Low-Decerebrate and in Spinal Cats After D-Amphetamine. Harriet M. Maling and G. H. Acheson. —p. 379.
Stimulation with Minimum Power. F. Offner.—p. 387.
Responses of Single Human Motor Units to Electrical Stimulation. E. Kugelberg and C. R. Skoglund.—p. 391.
Natural and Artificial Activation of Motor Units—A Comparison. E. Kugelberg and C. R. Skoglund.—p. 399.
Competitive Reinnervation of Rat Muscles by Their Own and Foreign Nerves. P. Weiss and Ann Hoag.—p. 413.

Journal of Nutrition, Philadelphia

32:121-226 (Aug.) 1946. **Partial Index**

*Some Effects of Dietary Oxalate on Teeth of White Rats. R. A. Gortner Jr., C. M. McCay, J. S. Restarski and C. A. Schlack.—p. 121.
Depletion of Hepatic Reserves of Vitamin A and Carotene in Cattle. P. R. Frey and R. Jensen.—p. 133.
Riboflavin Excretions of Young Women on Diets Containing Varying Levels of B Vitamins. Margaret V. Davis, Helen G. Oldham and Lydia J. Roberts.—p. 143.
Isoleucine, Leucine and Valine Requirements of Chick. C. R. Grau and D. W. Peterson.—p. 181.
Pantothenic Acid Content of Blood and Tissues of Chicken as Influenced by Level in Diet. P. B. Pearson, V. H. Melass and R. M. Sherwood. —p. 187.
Effects of High Fat Diet in Temperate Environment. F. C. Consolazio and W. H. Forbes, with technical assistance of S. P. Taylor, J. Poulin, M. Castiglione and J. Stachelek.—p. 195.
Effect of Excess Dietary Calcium on Longevity and Tissue Calcium in Albino Rat. J. B. Shields and H. H. Mitchell.—p. 213.

Dietary Oxalate and Rat's Teeth.—Gortner and his associates demonstrated that ingestion of solutions of various food acids (phosphoric, citric, lactic, sulfuric) caused considerable destruction of rat molars. They found in feeding experiments on young white rats that small amounts of soluble oxalate in the food or drink produced a hard deposit on the teeth of the animals which grossly resembled human dental calculus. The extent of this encrustation, which is presumably calcium oxalate, varied with the concentration of oxalate consumed and with the length of the experiment. Because of this phenomenon, oxalic acid solutions did not etch the enamel of the teeth of rats, in contrast to the action of other common food acids (citric, lactic, phosphoric, sulfuric). When oxalic acid or its sodium salt was present in the rat's food or drink the decalcification of teeth which accompanies ingestion of phosphoric (0.055 per cent) and citric (0.20 per cent) acid solutions diminished or disappeared. Protection against the etching action of orange juice was afforded by a concentration of 0.1 per cent oxalate in the juice.

Journal of Urology, Baltimore

56:151-270 (Aug.) 1946

Study of Experimental Urinary Calculi: III. Persistence of Stone Forming Tendency in Estrogen Treated Male Rats and Its Relation to Diet. J. G. Wilson, Alice D. Leahy and J. A. Benjamin.—p. 151.
Horseshoe Kidney in Pregnancy. R. Bell.—p. 159.
Large Pyelogenic Cyst with Crossed Renal Ectopia. H. H. Lerner and A. I. Gazin.—p. 162.
Pelvic Fused Kidney with Surgical Removal of Calculi: Case. H. R. Newman.—p. 169.
Renal Ectopia: Demonstration of Crossed Unfused Ectopia by Fluoroscopy. B. Resnick and J. H. Clark.—p. 173.
Supernumerary Kidney as Cause of Ureteropelvic Obstruction. H. E. Carlson.—p. 179.
Cavernous Hemangioma: Renal Vascular Tumor Requiring Nephrectomy; an Unusual Entity. W. White and L. E. Braunstein.—p. 183.
Hypernephroma in Polycystic Kidney. W. G. Hayward.—p. 190.
Mammoth Kidney Stone: Case. I. G. Duncan.—p. 193.
Spontaneous Rupture of Urinary Bladder. W. M. Feigal and J. A. Polzak.—p. 196.
Infiltrating Carcinoma of Bladder: Histologic Pattern and Degree of Cellular Differentiation in 97 Autopsy Cases. H. J. Jewett and S. S. Blackman.—p. 200.
Urologic Complications Following Operation for Imperforate Hymen. C. M. Crigler.—p. 211.
Regeneration of Epithelium of Prostatic Urethra Following Resection. N. E. Berry and J. Miller.—p. 223.
Rupture of Urethra, New Diagnostic Sign. V. Vermooten.—p. 228.
Repair of Hypospadias and Urethral Fistula. A. B. Cecil.—p. 237.
Balanitis Xerotica Obliterans. A. G. Franks.—p. 243.
Nonparasitic Chyluria with Special Reference to Traumatic Chyluria. J. A. Lazarus and M. S. Marks.—p. 246.
Experiences with Intravenous Urography in General Hospital in India. C. M. Norfleet Jr. and P. J. Hodes.—p. 259.
Investigation of Spermatogenic Function of Testicles in Cases of Azoospermia. M. Huhner.—p. 266.

Kentucky Medical Journal, Bowling Green

44:239-278 (Aug.) 1946

President's Address: The Neglected Patient. W. A. Weldon.—p. 242.
Practical Points in Diagnosis and Treatment of Squint in Children. G. P. Guibor.—p. 244.
Causes and Distribution of Blindness in Kentucky Among Recipients of Aid to Needy Blind. R. Sory and F. W. Caudill.—p. 255.
Contusion Injuries of Globe. C. D. Townes.—p. 264.
Recent Developments in Use of Penicillin and Sulfonamides in Treatment of Diseases of Ear, Nose and Throat. K. N. Victor.—p. 266.
Treatment of Dendritic Keratitis. W. C. Wells.—p. 269.
Catarrhal Deafness. W. S. Snyder.—p. 272.
The Village Doctor. E. L. Smith.—p. 274.

Medical Annals of District of Columbia, Washington

15:363-412 (Aug.) 1946

Treatment in Psychiatry. A. M. Duval.—p. 363.
Recent Trends in Therapy of Liver Disease. L. J. Thomas.—p. 375.
Recent Advances in Anesthesiology. D. Stubbs.—p. 381.
Virus Pneumonia: Differentiation from Pulmonary Tuberculosis. P. R. Wilner.—p. 385.

15:413-472 (Sept.) 1946

Recent Developments in Neurology and Psychiatry. S. Katzenelbogen. —p. 413.
Penicillin Therapy in Practice of Internal Medicine and Pediatrics. Georgine Rotman-Kavka, H. L. Hirsh, H. F. Dowling and L. K. Sweet.—p. 420.
Papillary Cystadenocarcinoma of Ovary. J. K. Cromer.—p. 425.
Expert Medical Witness. J. A. Gannon.—p. 429.

Michigan State Medical Society Journal, Lansing

45:999-1134 (Aug.) 1946

New Anti-Histamine Drugs in Allergic Diseases. G. L. Waldbott. —p. 1051.
*Experiment in Free Chlorination of Public Water Supplies. W. DeKleine and R. J. Faust.—p. 1055.
Imported Tropical Disease—Community Problem. M. Dale.—p. 1057.
Medicine and Industrial Research. C. F. Kettering.—p. 1063.

Free Chlorination of Public Water Supplies.—DeKleine and Faust discuss the advantages of "free chlorination," more generally known as breakpoint chlorination, which is the treatment of public water supplies that has been introduced in a number of Michigan communities. They cite the case of a small

city in western Michigan where the source of the water was an inland lake. Algae and weed growth were luxuriant. This unfiltered water was treated with the usual amount of chlorine, about 1.5 parts per million, and also about 0.1 part per million of ammonia. This provided a chloramine (combined chlorine) residual of between 0.3 and 0.5 part per million at the pumping station. The resulting tastes were so objectionable that the residents had to depend largely on bottled water for drinking purposes. It was recommended that the ammonia application be discontinued and that the chlorine treatment be increased in an amount sufficient to produce a residual of free chlorine.

Pennsylvania Medical Journal, Harrisburg

49:1305-1496 (Sept.) 1946

Psychosomatic Aspects of Arterial Hypertension. E. Weiss and M. Kleinbart.—p. 1321.
Operation for Chronic Dacryocystitis (Plastic Dacryocystorhinostomy). R. G. Hamilton.—p. 1327.
Evaluation of Blood Protein and Factors in Atopic Eczema. Patricia Drant.—p. 1331.
Treatment of Epidemic Diarrhea of Newborn. R. H. High.—p. 1334.

Psychiatric Quarterly, Utica, N. Y.

20:183-370 (April) 1946

Method of Resolving Acute Catatonic Excitement. J. N. Rosen.—p. 183.
Carl Gustav Jung—Defender of Freud and the Jews: Chapter of European Psychiatric History Under Nazi Yoke. E. Harms.—p. 199.
Benign Intracranial Space-Occupying Masses Simulating Mental Disorders. R. D. Whitfield.—p. 231.
Lure of the Supernatural. N. Fodor.—p. 253.
Fear. J. A. Brussel.—p. 269.
Management of Psychiatric Patients in Combat Area. T. E. Newell.—p. 275.
Psychopathology of Compulsive Smoking. E. Bergler.—p. 297.
Group Therapy in Extramural Clinic. Katherine W. Wright.—p. 322.

Surgery, Gynecology and Obstetrics, Chicago

83:289-416 (Sept.) 1946

Unusual Metastatic Manifestations of Breast Carcinoma: I. Metastasis to Mandible, with Report of 5 Cases. F. E. Adair and J. B. Herrmann.—p. 289.
Pelvic Floor in Parturition. R. M. H. Power.—p. 296.
Evaluation of Certain Drugs Used to Maintain Blood Pressure During Spinal Anesthesia: Comparison of Ephedrine, Paredrine, Pitressin-Ephedrine and Methedrine in 2,500 Cases. R. D. Dripps and Margery Van N. Deming.—p. 312.
*Use of Tyrothricin in Surgical Infections. D. D. Kozoll, K. A. Meyer, W. S. Hoffman and S. Levine.—p. 323.
*Identification of Clostridium Welchi in Mixed Cultures and Debrided Tissue and Determination of Sensitivity of Organism to Penicillin. G. Heller, M. E. Freeman, N. H. Shope and R. H. Kindrick.—p. 343.
Repair of Vesicovaginal Fistula Caused by Radiation. G. H. Twombly and V. F. Marshall.—p. 348.
Mandibular Tumors: Clinical, Roentgenographic and Histopathologic Study. L. T. Byars and B. G. Sarnat.—p. 355.
Cherney Incision as Applied to Surgery of Lower Ureter and Bladder. D. R. Smith.—p. 364.
Exposure of High Lesions of Sciatic Nerve. I. Aird.—p. 369.
Cineplastic Forearm Amputations and Prostheses. B. K. Rank and G. D. Henderson.—p. 373.
Effect of Pulmonary Resuscitative Procedures on Circulation as Demonstrated by Use of Radioactive Sodium. S. A. Thompson, Edith H. Quimby and Beverly C. Smith.—p. 387.
*Cancellous Bone Grafts for Infected Bone Defects: Single Stage Procedure. H. M. Coleman, J. E. Bateman, G. M. Dale and D. E. Starr.—p. 392.
Outlet Pelvimetry: Commentary, and Presentation of Pelvimeter for Measuring "Symphysis and Sacral Biparietal Distance." H. Thoms.—p. 399.

Tyrothricin in Surgical Infections.—Kozoll and his associates say that tyrothricin which contains both gramicidin and tyrocidin could combine the bacterial potency of the fomer with the stability and solubility of the latter. They studied the clinical effectiveness of tyrothricin by using it as a wet dressing in treating 77 patients with surgical infections, the majority of whom had failed to respond to other methods. Fifty of the 77 patients had excellent clinical results, 8 had fair clinical results and 19 had poor results. Tyrothricin, when used on one of the bilateral lesions in 6 cases, produced in 5 either a more rapid rate of healing, less pain and exudate, or a greater bactericidal effect than control measures in the contralateral lesion. It was most effective in hemolytic streptococcus lesions, next in those with Staphylococcus aureus and albus. It was ineffective when the preponderant organisms were gram negative. Tyrothricin appeared to encourage the growth of pseudomonas, pyocyaneus and diphtheroid organisms, but it did not produce anemia or hemolysis. Tyrothricin treatment was associated with mild skin reaction in 3 patients; these reactions disappeared when treatment was discontinued in 2 instances, and in spite of continuation of therapy in the third. Tyrothricin is recommended as a nontoxic, noninjurious antibiotic agent for local use in the treatment of surgical infections, if the wound is open, if there is adequate surgical drainage, if there is adequate blood supply and if the predominant organisms are streptococci or staphylococci or both.

Identification of Clostridium Welchi and Determination of Sensitivity to Penicillin.—Heller and his associates show that a rapid bacteriologic method for identifying gas gangrene organisms may be an aid in the management of contaminated wounds. At their laboratory the production of acrolein from glycerol has been used as the basis for a rapid test for Clostridium welchi. This procedure depends on (1) the aerobic growth of anaerobes in a specially prepared medium, (2) the development of acidity which determines the testing time for acrolein and (3) the testing for acrolein in the culture medium with a standardized Schiff's reagent. The inhibition of acrolein by the penicillin in the medium was taken as a measure of penicillin sensitivity.

Cancellous Bone Grafts for Infected Bone Defects.—Coleman and his associates, over the past fourteen months, have cleaned out 52 infected bone defects, filled them with cancellous chip grafts and closed them without drainage. The patient is treated with 20,000 units of penicillin intramuscularly every three hours, two days before operation. This is continued postoperatively until his temperature has remained normal from two to five days. At operation all scar tissue, granulation tissue and sequestrums are removed. The cavity is excised with an osteotome or curetted down to healthy bleeding bone. The wound is washed out and penicillin sulfathiazole powder is sprinkled liberally. The grafts are taken from the iliac crest. A trap door of cortical bone with attached periosteum is raised from the crest of the ilium. A wedge of cancellous bone can then be cut and further bone obtained with a curet. The wedge of cancellous bone is shaved with a sharp osteotome into thin chip grafts. The cavity is filled with chips and penicillin powder held together with coagulated autogenous plasma. One to 2 cc. of 0.2 per cent sterile agar is added as a coagulant. The tibia was involved in 29 cases, the femur in 12, the os calcis in 3, the humerus in 6, the carpus in 2. In all 52 cases infection was present at the time of operation, but no virulent infections have resulted and there has been no flare-up of infection after healing for periods up to fourteen months. The one stage method for obliterating infected bone defects saves months of hospital treatment and restores function before changes from disuse become irremediable.

Texas State Journal of Medicine, Fort Worth

42:301-350 (Sept.) 1946

Diagnosis of Liver Abscess by Means of Thorotrast Hepatosplenography. R. J. Reeves and K. A. Youngstrom.—p. 310.
*Para-Aminobenzoic Acid in Treatment of Endemic Typhus Fever. M. D. Levy and W. T. Arnold.—p. 314.
Prostigmine Usage in Pediatrics. G. A. Title.—p. 316.
Water in Relation to Health Problems in Children in Texas. A. E. Hansen.—p. 320.
Cleaning Traumatic Wounds by Multiple Fine-Stream Pressure Irrigation—Improved Method. J. P. Barnes.—p. 322.
Management of Prostatic Surgery in the Aged. J. P. Bridges.—p. 325.
Primary Carcinoma of Gallbladder. F. J. Kelly and T. Speed.—p. 327.
Fungus Infections of Cornea: Case Report of Keratomycosis Due to Monilia. E. M. Sykes.—p. 330.
Epidemiologic Investigation of Typhus Fever in Texas, 1943-1945. J. V. Irons and G. W. Cox.—p. 332.
Teamwork in Cancer Control. J. L. Neff.—p. 336.

Para-Aminobenzoic Acid in Endemic Typhus.—According to Levy and Arnold murine typhus is endemic in Texas and has considerably increased. They report 6 cases of murine typhus observed in the Medical Service of the Southern Pacific Hospital in Houston, Texas. The diagnosis was made on clinical symptoms and findings and by the determination of the Weil-Felix reaction. Since para-aminobenzoic acid inhibits the growth of rickettsiae and had proved effective in an epidemic of louse borne typhus fever, the authors used it in the aforementioned 6 cases, administering 2 Gm. every two hours. The drop in temperature and relief of symptoms were almost dramatic in their effect. No side effects were noted.

FOREIGN

An asterisk (*) before a title indicates that the article is abstracted below. Single case reports and trials of new drugs are usually omitted.

British Journal of Radiology, London

19:349-392 (Sept.) 1946

Dose Measurement in Beta Ray Therapy. G. W. Bloomfield and F. W. Spiers.—p. 349.
Dose Measurements with Radium Beta Ray Applicators. G. J. Neary. —p. 357.
New Units for Measurement of Radioactivity. E. U. Condon and L. F. Curtiss.—p. 368.
*Pyridoxine in Treatment of Radiation Sickness. L. M. Shorvon.—p. 369.
Moscow's X-Ray Services. R. Golonzko.—p. 371.
Radiologic Demonstration of Regression of Retroperitoneal Hodgkin's Disease. H. Cohen.—p. 372.
Subacute Ileoileal Intussusception in Adult: Case Report. E. Tiscenco. —p. 374.
Wrist Injuries in Service Patients. F. Pygott.—p. 381.
X-Ray Appearances of Pharyngeal Palsy. B. Mannheimer.—p. 383.
Leontiasis Ossea. W. Tennent.—p. 388.

Pyridoxine in Radiation Sickness.—According to Shorvon pyridoxine is a member of the vitamin B group occurring principally in liver and yeast. It can be obtained in tablets for oral use and in ampules for intravenous medication. The author employs the tablets, giving five 10 mg. tablets daily. Occasionally he gives intravenous injections of two ampules (each containing 50 mg.) a week. In addition to its value in the treatment of radiation sickness, it increases the leukocyte count. This is of importance because of the tendency for x-rays to depress the white cell count. The author used pyridoxine in the treatment of 24 cases of radiation sickness. Good results were obtained in 22 of these.

British Medical Journal, London

2:288-318 (Aug. 31) 1946

*Tobacco and Ulcer Dyspepsia. R. A. Jamieson, C. F. W. Illingworth and L. D. W. Scott.—p. 287.
Electroconvulsion Therapy in 301 Patients in General Hospital, with Special Reference to Selection of Cases and Response to Treatment. D. E. Sands.—p. 289.
*Technic for Use of d-Tubocurarine Chloride with Balanced Anaesthesia. T. C. Gray and J. Halton.—p. 293.
Some Uses of Thrombin in Surgery of Ear, Nose and Throat. P. Reading.—p. 295.
Staphylococcic Spinal Osteomyelitis with Acute Extradural Abscess. G. Blackburn and R. P. Jepson.—p. 297.

Tobacco and Ulcer Dyspepsia.—Jamieson and his associates report a follow-up survey of 473 patients who had suffered acute perforation of a peptic ulcer from one to five years previously. They were recalled for examination and were closely questioned about their smoking habits. Heavy cigaret smoking was associated with severe symptoms, but pipe smoking with mild symptoms. It is suggested that the relationship between smoking and severity of symptoms is indirect and depends on age: symptoms tend to be severe in the young and mild in the old. Cigaret smokers are in the main young, while pipe smokers are in the main old. There was no evidence that increase or decrease in tobacco consumption influenced the severity of symptoms.

Curarine with Balanced Anesthesia.—Gray and Halton state that this anesthesia is suitable for all endoscopic investigations, but particularly for bronchoscopy and esophagoscopy by virtue of the complete relaxation of the vocal cords and the pharyngeal sphincter. A single injection of 15 mg. of curarine (d-tubocurarine) is followed by a suitable dose of a barbiturate, both given intravenously. Administration for longer procedures is essentially a balanced anesthesia. After induction the patient is maintained in a light plane by means of an intravenous barbiturate. The author stresses that curare should not be considered merely as an "aid" to anesthesia: it is an integral part of the anesthetic procedure. This is by virtue of four important properties: (*a*) It is quickly eliminated, leaving no toxic aftereffects; (*b*) it produces relaxation as and when desired; (*c*) it abolishes laryngeal and bronchial spasm, making intubation of the trachea necessary only in selected types of cases; (*d*) because of the undoubted synergistic action with the anesthetic agents, the dose necessary to keep a patient asleep can be considerably reduced. If these four properties are borne in mind, and if a correctly balanced anesthesia is maintained, patients after long abdominal and thoracic operations are awake, in good vasomotor equilibrium, free from nausea and able to exert their respiratory functions to the full. There is in consequence a smooth postoperative convalescence.

Journal of Physiology, Cambridge

105:1-94 (July) 1946. **Partial Index**

Effect of Dietary Restriction on Incisor Teeth of Rachitic Rats. J. T. Irving.—p. 16.
Presence of Sympathomimetic Substance in Extracts of Mammalian Heart. U. S. v. Euler.—p. 38.
Distribution of Excitation and Inhibition in Single Fiber Responses from Polarized Retina. R. Granit.—p. 45.
Investigation for Presence of Skin Protease Inhibitory Factor in Burned Skin. A. Beloff and R. A. Peters.—p. 54.
Changes in Intestinal Tone and Motility Associated with Nausea and Vomiting. R. A. Gregory.—p. 58.
Observations on Plasma Volume Estimations with Dye T 1824. E. B. Reeve and J. Armin.—p. 72.

Medical Journal of Australia, Sydney

2:109-144 (July 27) 1946

Behavior of New Guinea Strains of Plasmodium Falciparum and Plasmodium Vivax when Cultivated in Vitro. R. H. Black.—p. 109.
Genitourinary Disorders Occurring in Singapore Prisoner of War Camp, with Special Reference to Polyuria and Nonspecific Inflammations. H. A. Phillips.—p. 111.
Profuse or Irregular Menstrual Periods in Young Women: Practical Program of Treatment. A. Grant.—p. 113.
*Advances in Surgery of Hand Infections, with Special Reference to Pad Infections. V. J. Kinsella.—p. 116.
Place of Surgery in Diseases of Chest. C. J. O. Brown.—p. 118.
Distribution of Fluorine in Potable Waters in New South Wales and Tasmania. R. L. Reid and N. D. Martin.—p. 121.

Surgery of Hand Infections.—Kinsella uses the term "pad infections" for the subcutaneous infections which tend to become localized in the palmar fatty pads. Pad infection I, the so-called felon, involves the distal phalangeal pad. Pad infections II and III involve the middle and proximal phalangeal pads respectively. Suppurative tenosynovitis may occur as a later complication. Pad infection IV involves the pads in the distal part of the palm and may spread to the web. It is usually due to infection occurring beneath a callosity, whereas infection in the first three pads is usually due to a puncture wound. Pad infections II and III may be distinguished from acute suppurative tenosynovitis; in acute suppurative tenosynovitis the swelling of the finger is uniform and the finger is sausage shaped; in pad infections the swelling is most pronounced over the affected pad, and the finger is spindle shaped. Incisions required to evacuate pus in pad spaces II, III or IV may be C shaped or cross shaped. The author uses for postoperative treatment the method which imitates the Winnett Orr technic. Dressings are changed infrequently, usually once a week. He regards the sulfonamides and penicillin as important additions. Erysipeloid infections occur in those handling fish and pigs. In these cases an ill defined area of inflammation spreads diffusely and irregularly from a slight injury. Operation is not indicated, for pus does not form. This infection is self limited.

Proceedings of Royal Society of Medicine, London

39:507-584 (July) 1946. **Partial Index**

*Treatment of Ulcerative Colitis with Intestinal Mucosa. A. M. Gill. —p. 517.
Observations on Etiology and Treatment of Sprue. A. L. Wingfield. —p. 519.
Tomography in Diagnosis of Lung Carcinoma. J. B. Hartley.—p. 531.
Observations on Radiology of Pancreas. R. A. K. Harper.—p. 534.
Problem of "Postmaturity." A. J. Wrigley.—p. 569.

Treatment of Ulcerative Colitis with Intestinal Mucosa.—Gill states that the cause of ulcerative colitis in some cases may lie in a deficiency caused by the lack of some factor produced by the small intestine. Treatment of some cases of ulcerative colitis with intestinal mucosa has given promising results. There is a latent interval of about three weeks before any appreciable improvement is noted. Mucosa taken from the different segments of the small intestine seems to be effective, although possibly jejunal mucosa produces a more lasting effect.

Presse Médicale, Paris

54:497-508 (July 27) 1946

Influence of Aminopyrine and of Salicylic Acid on Natural Vegetative Factors; Therapeutics for Rheumatism and for Anaphylactic Accidents. Danielopolu, M. Popesco and D. Crivetz.—p. 497.
Statistical Evidence in Surgical Treatment of Arteritis Obliterans of Limbs. P. Wertheimer and R. Gauthier.—p. 497.
Neurosurgical Point of View in Cerebral Edema. J. A. Chavany and G. Guiot.—p. 499.
Small Umbilical Hernia of Infants; Indications for Surgical Treatment and Technic. M. Fèvre and J. R. Barcat.—p. 500.
*Twenty Years of Treatment of Diabetes Insipidus by Nasal Administration of Powdered Posterior Lobe of Pituitary. A. and Lucie Choay. —p. 500.

Treatment of Diabetes Insipidus by Nasal Administration of Powdered Posterior Lobe of Pituitary.—The Choays have used this method for twenty years to control thirst and polyuria in more than 100 cases of diabetes insipidus. The powder is obtained by pulverizing and sifting posterior lobes of beef pituitary glands previously dried in a vacuum and in the presence of sulfuric acid or dehydrated by acetone. One ox supplies about 0.08 Gm. of powder, i. e. about one daily dose. The powder is taken into the nose in the same manner as snuff. The patient should blow his nose prior to the administration of the powder but should not blow his nose or sneeze for several minutes afterward. The best results were obtained with three to five doses of 0.01 Gm. in the course of one day and with 1 dose of 0.02 Gm. at night before going to bed. In cases of severe polyuria, mixed treatment by nasal administration of powder during the day and by an injection of 10 mg. at night is suggested. In the average case the effect of the powder when administered correctly to a healthy nasal mucosa lasted for three to six hours during the day and for six to ten hours during the night. The contraindications to the method are hypertrophic rhinitis, chronic rhinorrhea and spasmodic rhinitis. Even a simple coryza may cause failure and favor local infection. Preliminary anterior rhinoscopy, therefore, is as important as a preliminary injection of the extract. Failure of nasal administration of the powder is to be expected in the case of failure of the preliminary injection.

Praxis, Bern

35:449-464 (July 11) 1946

*Endocrine Treatment of Carcinoma of Prostate. G. Reimann-Hunziker. —p. 449.
The Notion of Alimentary Equilibrium in Daily Practice. L. M. Sandoz. —p. 452.

Endocrine Treatment of Carcinoma of Prostate.—According to Reimann-Hunziker only radical operation of a carcinoma of the prostate brings prospects of a complete cure. This treatment is rarely possible because the patients come under medical care too late. All other treatments are merely palliative. Castration and estrogenic therapy may prolong life and in many cases pains and dysuria may temporarily disappear. Improvement is usually most rapid if castration is followed by a transurethral electroresection with subsequent protracted medication with diethylstilbestrol. With this combined treatment the longest average survival is obtained. Occasionally improvement of the general condition is so good that the patient may be able to work again for a while. The primary tumor as well as the metastases may regress. However, neither castration nor estrogenic therapy will prevent metastatization. Improvement is always only temporary and persists for only about six months or somewhat longer. The hope that the tumor might regress sufficiently so that it might become operable has not been realized. The determination of the serum phosphatase will, if it is positive, give information about the prognosis and the efficacy of a treatment. A high phosphatase value suggests bone metastases.

Revista Méd.-Quirúrg.de Patol. Femen., Buenos Aires

14:71-128 (April) 1946. **Partial Index**

*Erythroblastosis of Newborn Infant with Rh Positive Mother Sensitized by Rh Factor. M. A. Etcheverry.—p. 83.

Erythroblastosis of Newborn Infant.—In 80 mothers of infants with erythroblastosis fetalis Etcheverry found the blood Rh negative in 69 (87 per cent) and Rh positive in 11 (13 per cent) of the cases. In 1 instance the blood of both parents and of the infant with the icteric type of erythroblastosis was of the O group and Rh positive. The blood subtypes were different, namely, Rh′ for the mother and RhO′ for the father and the infant. Anti-Rh antibodies of Anti-RhO specificity were encountered in the mother's blood. Successful therapy consisted in blood transfusion every three days up to a total of five transfusions, for which blood of the group, type and subtype of those of the mother was used. Injections of vitamin K and of liver extract were also administered to the infant.

Acta Medica Orientalia, Jerusalem

5:177-208 (June) 1946

Further Observations on Enhanced Fragility of Red Cells in Malaria Patients. D. Birnbaum, N. Goldblum and I. J. Kligler.—p. 177.
*Penicillin Through Duodenal Tube in Gastric Surgery. J. Dwek and F. Mandl.—p. 185.
Influence of Buffer Solutions on Gastric Acidity. M. Grotto.—p. 190.
Rare Case of Thromboangiitis Obliterans. B. Neumann.—p. 197.
Laboratory Improvements in Microbiochemistry. F. Rappaport and F. Eichhorn.—p. 199.

Penicillin Through Duodenal Tube in Gastric Surgery.—Dwek and Mandl point out that the acidity of the gastric juice is reduced after operations on the stomach because of the removal of the hydrochloric acid producing glands in subtotal gastrectomy and the regurgitation of the alkaline bile into the stomach after a well functioning gastroenterostomy. They administered penicillin through the duodenal tube to 7 patients, to 4 after subtotal gastrectomy and to 3 after gastroenterostomy. The dosage varied, some patients being given doses of 12,500 and 6,500 units, others several doses of 25,000 or 50,000 units and still others a single dose of 100,000 units. The level of penicillin in the blood serum was within the therapeutic range in 5 of the patients. The duodenal tube method avoids the unpleasant effects of the numerous injections necessary with the parenteral route of administration.

Nordisk Medicin, Gothenburg

30:1037-1084 (May 10) 1946. **Partial Index**

Supravesical Hernias. I. C. Højensgaard.—p. 1037.
Experiences in After-Treatment of Amputation Stumps. L. Hagelstam. —p. 1040.

Hospitalstidende

*Investigations on Course of Scarlet Fever, Its Complications and Their Treatment in Five Year Period, with Special Regard to Effect of Scarlet Fever Convalescent Serum in Preventing Complications. I. Søndergaard.—p. 1043.

Duodecim

Nature of Paranoia. L. Saarnio.—p. 1051.
Screw Traction Apparatus for Humerus. K. R. Inberg.—p. 1059.

Norsk Magasin for Lægevidenskapen

Hemihypertrophy. L. Gram.—p. 1061.
Fatal Poisoning with Sodium Silicofluoride (Rat Poison). A. S. Johannessen—p. 1065.

Hygiea

Thiouracil Treatment of Exophthalmic Goiter with Complications. H. Lindholm.—p. 1071.
Unique Case of Hemangiolymphangioma in Broad Ligament of Uterus. O. Johansson and Åke G. H. Lindgren.—p. 1073.

Scarlet Fever and Its Complications.—In 1,061 cases of scarlet fever from 1940 to 1944 in patients aged from 6 months to 65 years the mortality was 0.2 per cent. Most cases occurred during the winter months. The frequency of complications seemed unrelated to the age. Lymphadenitis occurred in 28 per cent, otitis media in 10 per cent, arthralgias in 7 per cent and nephritis in 3 per cent of the cases. Søndergaard states that early treatment with scarlet fever convalescent serum did not prevent complications; sulfanilamide early in the course perhaps reduces the number of complications. Erysipelas and otitis media should be treated with sulfanilamide or sulfathiazole; in lymphadenitis their effect is doubtful. Application of these agents in treatment of the other complications appears useless. The high sedimentation reactions are caused mainly by the arthralgias, the long periods of hospitalization mostly by nephritis and otitis media.

Book Notices

Diabetes: A Concise Presentation. By Henry J. John, M.A., M.D., F.A.C.P. Cloth. Price, $3.25. Pp. 300, with 74 illustrations. St. Louis: C. V. Mosby Company, 1946.

This book represents the accumulated interest of its author, whose experience has been large and intensive. It contains much that is sensible and good, and even when the reader will feel that he cannot subscribe to the author's dicta he will still be indebted to him for having challenged his point of view. The volume is not an all inclusive discussion of the subject of diabetes. It is intensive in some phases and passes lightly over other phases of the subject. That to a certain extent is inevitable in any monograph. It would be more apt to appeal to the seasoned practitioner than to a student of medicine, and yet the practitioner who is not experienced in the handling of diabetic patients also needs systematized guidance and approach. When all is said and done, in dealing with the description of a disease it is best accomplished by considering its etiology, pathology, symptoms, diagnosis, complications and treatment in classic nosographic style. No one has yet found a better way. When this systematization is ignored, whether each chapter or section is designated as such is not as important as is a logical sequence in the presentation. Otherwise the usefulness of a book may be definitely impaired because valuable passages and observations may be misplaced and remain unnoticed. John has devoted a medical lifetime to diabetes, and his book describes many of the ins and outs of the subject. His book is a greater contribution to the subject of diabetes than that of the publisher to the art of bookmaking. This shortcoming can be charged only in part, to the war and its aftermath.

Nursing and Nursing Education. By Agnes Gelinas, R.N., A.M., Professor of Nursing and Chairman of the Skidmore College Department of Nursing—New York Post-Graduate Medical School and Hospital, New York. Studies of the New York Academy of Medicine, Committee on Medicine and the Changing Order. Cloth. Price, $1. Pp. 72. New York: Commonwealth Fund; London: Oxford University Press, 1946.

Consistent with the type of book sponsored and published by the Commonwealth Fund, this edition has the meat of the problem clearly stated. It is a surprisingly small volume for so much information. A brief summary of past developments precedes the outlining of contemporary problems with the advice "Nor is the maintenance of standards, once they have been attained, sufficient: to have reached a goal is commendable, but the ground gained must be held and new ground won." The necessity of changes in present day educational methods is justified by the choice of a few but exceptional statistics which drive the points home. Future developments indicate that a larger number of qualified nurses will be needed during the next ten years than has ever been experienced before in our country. The demand is really being exerted now—before an adequate number of specially trained nurses can be supplied for the specialties that are developing in nursing as they have developed in the practice of medicine. Estimates indicate that 355,000 graduate nurses will be available in 1948, but the postwar requirements for the country call for 485,600 full time registered professional nurses. The need for larger classes in the face of elevation of educational standards is obvious.

Recreation and the Total Personality. By S. R. Slavson. Cloth. Price, $3. Pp. 205. Association Press, 347 Madison Ave., New York 17, 1946.

There are few books to date which put recreation into perspective as a derivative of man's basic nature as does this publication. This postwar volume is most timely, because in these days of reduced work hours, automatic labor and time saving devices, leisure time is on the increase. How can recreation make its maximum contribution to the total well-being and wholesome living of individuals and communities? Practitioners, recreationists, educators, sociologists, community organization leaders, social and group workers, hospital and institution staffs, parents-teachers, work foremen and the general community will do well to read this book, as from it emerges a concept of recreation embracing the insights of mental hygiene, education, psychology, sociology, social work and group work. The ten chapters which comprise the book are on the nature and scope of recreation, unconscious motivations, fitting recreation to the individual, recreation and the democratic culture, the problem of competition, a demonstration of the new recreation, constants, variables and differentials, leadership and recreation, supervision: a creative relation, and community resources. The author suggests technics that lean less on a stock of artifices, games and facilities and more on an individualization that will balance the deprivations from which we suffer, such as physical underfunctioning, frustration of unconscious drives, devaluated self esteem, lack of self assertion and inadequate creative expression. Recreation is a part of the total educational experience of man in modern society. Its value can be realized only when some traditional views of recreation are modified or eliminated.

Eléments de psycho-physiologie. Par Henri Roger, professeur honoraire de physiologie à la Faculté de médecine de Paris. Paper. Price, 350 francs. Pp. 428, with 20 illustrations. Masson & Cie, 120 Boulevard Saint-Germain, Paris 6e, 1946.

This book, written by a French physiologist, purports to put psychology on a sound and scientific basis. It is too voluminous for an introduction and much too superficial for a textbook, besides lacking bibliography or index. Heavily weighted in favor of French literature, it starts out with a short reflexology, not taking into account modern research on reflexes of posture, vestibular reflexes, and so on. This is followed by a purely descriptive treatment of instincts, of which the author seems to recognize about six: the instincts of alimentation, defense, reproduction, motherliness, gregariousness and migration. He also mentions an instinct of play. In the following part the intellectual acts are based predominantly on cerebral function. The emotions are treated descriptively. The author differentiates between primary emotions (fear, anger and love) and secondary emotions, under which heading one finds a motley assembly such as feelings of justice, of religion, of beauty. Of gestalt psychology, analytic psychology, the author has only the vaguest notion. The few times he mentions Freud he misquotes him (for instance, accusing him of reducing all instincts to the reproductive one or ascribing the causes of all dreams to the unconscious memory of erotic stimulations). In the final part, on psychophysiologic functions, one finds a treatise on determinism and freedom, chapters on heredity, periodicity (including a short review on electroencephalography), sleep and dreams, and 20 pages on consciousness and the unconscious acts, omitting, of course, the large body of research on the dynamics of the unconscious.

Endoscopia normal de la uretra membranosa y del cuello del bulbo. Por Hector Diaz Castro, profesor agregado de urología de la Facultad de medicina de Montevideo. Este trabajo fué presentado como tesis al concurso para profesor agregado de urología de la Facultad de medicina. Paper. Pp. 151, with 55 illustrations. Imprenta "Rosgal," de Hilario Rosillo, Montevideo, Uruguay, 1944.

In contradistinction to the extensive studies reported on the anatomy of the prostatic and anterior urethra, the membranous urethra and bulbar urethra seem to have been neglected. Nor do existing descriptions correspond accurately with the actual morphologic and anatomic conditions observed endoscopically. The author presents his own conception based on several years' study of the region, which is influenced throughout most of its course by the interplay of muscles and the intricate complex composed of the musculoaponeurotic combination known as the urogenital diaphragm. The dynamic character of the area renders cadaver studies misleading, the postural variations due to muscular activity producing transitory morphologic changes. In the cadaver the urethral muscle is fixed. Endoscopy of the urethra has hitherto been largely limited to the prostatic and anterior urethra and verumontanum, the sites of predilection for most tumors and inflammatory changes. After reviewing the classic conceptions based on the anatomic studies on the cadaver, the author proceeds to describe the technic for endoscopy of this particular region and presents certain anatomic and physiologic deductions based thereon. Following a review of endoscopic findings, these are compared with the histologic anatomic findings in various stages of embryologic life and in the adult.

The endoscopic images are all interpreted in relation to roentgenograms of the normal states of dilatation and contrac-

tion: The physiology of the membranous urethra and neck of the bulbar urethra is explained, including a discussion of sympathetic and voluntary innervation, the special physiology of the membranous urethra, of the bulbar genital function in ejaculation. Also the physiopathology of the membranous urethra in neurogenic hypertonic and hypotonic vesical disturbances is demonstrated, as well as their endoscopic aspects. It is emphasized that the canalicular and muscular systems form an inseparable complex of primary and accessory muscles controlled by the sympathetic and voluntary nervous system. The interbulbomembranous sheath serves as a point of fixation for the urethra and as a support for its motor muscle. He concludes that almost the entire dynamism of the membranous urethra is located in the median portion of the inferior wall, which he describes as the poculiform portion. The other portions play a much less significant physiologic role. In the final chapter he discusses the extremely rare congenital malformations of the membranous and bulbar urethra, with a description of 2 cases.

Disorders of the Blood: Diagnosis, Pathology, Treatment and Technique. By Sir Lionel E. H. Whitby, C.V.O., M.C., M.D., Regius Professor of Physic in the University of Cambridge, Cambridge, and C. J. C. Britton, M.D., D.P.H., Assistant Pathologist, The Bland-Sutton Institute of Pathology, The Middlesex Hospital, London. Fifth edition. Fabrikoid. Price, $10. Pp. 665, with 86 illustrations. Philadelphia: Blakiston Company, 1946.

In preparing the fifth edition of their widely known work the authors have made extensive revisions in the chapters dealing with the origin and development of the blood cells, the hemolytic anemias, the anemias of infancy and childhood, agglutination of the red blood cells and blood transfusion and technic. The text has been lengthened, and there are some new colored illustrations of the bone marrow. Although greatly disturbed by the war, the authors have nevertheless done their utmost to keep the material up to date. This has been particularly difficult in view of the rapidly changing views regarding the Rh factors. Much of the best research on the blood is now being carried on in laboratories in the United States, and much which was not easily available during the war is now becoming for the first time common knowledge. The authors have done a great deal to acquaint themselves with recent advances in the United States, but a new edition will probably be necessary within a short time if all essential new information is to be added.

Principles of Radiography. By C. B. Minnich, B.Sc., R.T. Fabrikoid. Pp. 130, with 43 illustrations. Kansas City, Missouri: The Author, 1946.

Because it contains essential elementary principles of the science of radiography in clear but concise form, this monograph makes an excellent handbook for the novice learning to operate x-ray equipment. Especially good is the review of the elementary physics of electricity and the description of the electrical setup of the x-ray machine. In addition, chapters on the subjects of radiation, the darkroom, the calibration, technical variations and x-ray protection are dealt with. This book was meant to be only a brief primer in basic study of x-rays and therefore does not concern itself with such topics as positioning, fluoroscopy or interpretation of x-ray films. Because it may be easily and quickly read and understood, the book is recommended to physicians who desire a summary knowledge of the physics of x-rays. It is highly recommended for use by student x-ray technicians.

Health from the Ground Up. By Karl B. Mickey. Paper. Pp. 125. Chicago: International Harvester Company, 1946.

Here is a provocative essay on the relationship between health and the soil in which food crops are grown. The author, who is in the public relations department of the International Harvester Company, believes that "exhaustion of the soil has been an important factor in the decline of civilizations" and that every effort must be made to secure more information on the relationship between the soil and human health. The material is well written, and there are many quotable statements throughout the book. An excellent bibliography of more formal treatments of the subject is appended.

The Results of Radium and X-Ray Therapy in Malignant Disease: Being the Second Statistical Report from The Holt Radium Institute, Manchester, Now Part of the Christie Hospital and Holt Radium Institute, Years 1934-1938 Inclusive, Assessed at 5 Years, and 1932 and 1933 Assessed at 10 Years. Compiled 1945 by Ralston Paterson, Margaret Tod and Marion Russel. Paper. Price, 7s. 6d. Pp. 147, with 3 illustrations. Edinburgh: E. & S. Livingstone, Ltd., 1946.

This is the second statistical report from the Holt Radium Institute, Manchester. The first part is a general survey of the treatment of cancer as a whole and is intended to interest the layman, the hospital administrator and the general practitioner. The second part is an evaluation of different methods of treatment. The technics are described and reference is made to publications in which may be found a full account of the physical principles together with detailed instructions for specialized methods. The third part refers briefly to the first report and gives a table showing the ten year results of treatment. The authors state that radium and x-rays are equally important, that each has advantages and that the two agents are often complementary. The tables are so arranged as to give the results of radiotherapy in various stages of the disease, thus permitting statistical comparison of different methods. The report represents a careful and complete study of the results of radiotherapy in a large group of cancers extending over a period of many years. It should be of interest to the physician as an indication of the role of radiotherapy in cancer as well as to the specialist, who is interested in the details of treatment. The research covered by the report constitutes a fundamental contribution to clinical cancer research.

Encyclopedia of Endocrinology. By Hans Selye, M.D., Ph.D., D.Sc., Professor and Diector of The Institute of Experimental Medicine and Surgery, University of Montreal. Section IV: Ovary. Volume VII (in two parts): Ovarian Tumors. Bibliography. Fabrikoid. Price, $21.75. Pp. 349, with 427 illustrations. Montreal: Richardson, Bond and Wright, 1946.

Dr. Hans Selye, convinced of the importance of the complete knowledge of the available literature for the study of any subject, began a long time ago to collect a library dealing particularly with endocrinology. His library now contains approximately 250,000 entries. The Encyclopedia is a step toward making that material generally available. The first publication was the "Classified Index of the Steroid Hormones and related Compounds," published in 1943. Now come two volumes on "Ovarian Tumors," which constitute part of section IV, which will be devoted to the ovary. The entire encyclopedia is to consist of ten sections covering all the glands of internal secretion. The encyclopedia is loose leaf, so that it may be kept up to date by the addition of new material. Every publication referred to is suitably indexed by number, so that reference may be had to the original source. The first two volumes are magnificently illustrated and written with an economy of style and diction highly commendable in a work of this type. There is a complete subject index and a bibliography of the periodicals concerned. The second volume is devoted wholly to the bibliography of ovarian tumors.

The Art of Medicine in Relation to the Progress of Thought: A Lecture in the History of Science Course in the University of Cambridge, February 10, 1945. By A. E. Clark-Kennedy, M.D., F.R.C.P., Physician to the London Hospital and Dean of the Medical School, London. Paper. Price, 75 cents. Pp. 48. New York: Macmillan Company; London: Cambridge University Press, 1945.

The publishers have made available in pamphlet form this lecture in the History of Science course. After reviewing briefly the progress of medical science, Dr. Clark-Kennedy concludes his address with a consideration of medicine and modern life. He fears the development of a medical science from which the humanities will have been lost. Thus he says "We live in an age in which scientific knowledge has outrun philosophy, narrow specialization is the order of the day, religion has ceased to be a unifying force in education, belief in the Christian revelation seems to have declined, and excessive anxiety over the health of the body has replaced preoccupation with the welfare of the soul. Humanity seems to be traveling through the night without any white line to keep us in the center of the road."

Queries and Minor Notes

THE ANSWERS HERE PUBLISHED HAVE BEEN PREPARED BY COMPETENT AUTHORITIES. THEY DO NOT, HOWEVER, REPRESENT THE OPINIONS OF ANY OFFICIAL BODIES UNLESS SPECIFICALLY STATED IN THE REPLY. ANONYMOUS COMMUNICATIONS AND QUERIES ON POSTAL CARDS WILL NOT BE NOTICED. EVERY LETTER MUST CONTAIN THE WRITER'S NAME AND ADDRESS, BUT THESE WILL BE OMITTED ON REQUEST.

NEWER FUNGICIDES

To the Editor:—**What new remedial measures are indicated in the treatment of epidermophytosis and other fungous infections? I have been informed that recent work by military organizations has resulted in the selection of remedies which are more or less specific in these cases.**

Edwin R. Watson, M.D., Macon, Ga.

ANSWER.—A number of promising therapeutic agents for the treatment of fungous infections have been adequately tried during the war years. The most important new development has been the use of mixtures of fatty acids and their salts such as sodium or calcium propionate-propionic acid mixtures. These compounds were found to be effective against human pathogenic fungi. They have also been used with good therapeutic results in otomycosis and oidiomycosis, thrush and blacktongue. The propionates are used in 10 to 30 per cent concentration in liquids, powders and ointments. Favorable results have also been reported following the use of undecylenate-undecylenic acid ointment. However, a number of observers have preferred the propionate-propionic acid preparations to the undecylenates. Evidence is accumulating which seems to indicate that mixtures of propionates and caprylates are the most effective of the fatty acids so far tried.

PROLONGED USE OF NASAL VASOCONSTRICTORS

To the Editor:—**What are the potential effects on the nasal mucosa of a vasoconstrictor such as neosynephrin administered daily for many months?**

M.D., Illinois.

ANSWER.—Several reports of undesirable effects from prolonged use of vasoconstrictor substances in the nose have appeared in literature in the past few years.

Experimentally the action of the cilia has not been depressed by such vasoconstrictor substances as ephedrine, neosynephrin, tuamine and some related substances in appropriate concentrations, and injurious effect to the mucosa has not been observed. While these drugs have had a therapeutic value in certain acute or subacute conditions, the prolonged use of at least two of the group (ephedrine and privine) has on numerous occasions been observed to cause an undesirable reaction in the nasal mucosa which is relieved only for a brief period by the vasoconstrictor effect. The mucosa becomes congested and has a diffuse dull red somewhat dry and irritated appearance and the airway is obstructed. Elimination of all intranasal medication in such cases has been followed by relief of symptoms within three to four days. A permanent pathologic change in the mucosa as a result of the use of vasoconstrictors has not been reported.

The cause of the congestion appears to be that the vasoconstrictor action is associated with irritation and is followed by vasodilatation and increased congestion.

Such a reaction frequently has been observed after the use of epinephrine, which has a strong vasoconstrictor effect. Repeated usage of vasoconstrictors produces a continuous state of irritation and mucosal congestion which can be termed a chronic rhinitis due to medicaments.

SCOPOLAMINE IN OBSTETRIC ANESTHESIA

To the Editor.—**Please discuss the use of scopolamine in obstetric anesthesia. Scopolamine 1/150 to 1/100 grain (0.4 to 0.6 mg.) as preanesthetic medication should reduce mucous secretions in the respiratory tract. If the time is short, it has been suggested that the drug be given intravenously in the same dosage. Will this procedure have untoward effects on the mother and/or the baby?**

M.D., Pennsylvania.

ANSWER.—Scopolamine in the dosage mentioned would certainly minimize mucous secretions. However, a smaller dose has been found adequate for the purpose even when given by hypodermic injection. There is no objection to giving scopolamine intravenously well diluted. One three-hundredth grain (0.2 mg.) or at most $\frac{1}{200}$ grain (0.3 mg.) has proved adequate. Neither this nor larger doses have any serious untoward effects on either mother or child. The accompanying psychic sedation is desirable. Larger doses do sometimes cause excessive dryness of the mucous membranes which is unpleasant to the mother.

SUN GLASSES

To the Editor:—**Please discuss the harmful or beneficial effects on the eyes of the average sun glasses sold in drug stores and dime stores throughout the country.**

Paul N. Taylor, M.D., Washington, D. C.

ANSWER.—Many poorly fitting and cheap glasses cause ocular distress and headaches; a person who has such distress when he wears glasses naturally takes them off, just as a man takes off a pair of shoes that do not fit him comfortably.

The light from which our eyes are protected by "sun glasses" may be considered as follows: (*a*) Sunlight: Very bright sunlight is distressing in varying degrees to all eyes. This is the reason why the eyelids are kept closed, or nearly closed, when one is facing such a light. (*b*) Ultraviolet: Ultraviolet light of the wavelength of approximately 300 millimicrons, such as is present in a rarefied atmosphere on high mountains or in dense snow fields, or such as comes from arc lights or welding machinery, causes irritation and temporary inflammation of the superficial cornea and conjunctiva, coming on eight to twenty-four hours after exposure and lasting a day or more. Welders, for instance, are protected by special goggles. (*c*) Infra-Red: Eclipse blindness is a burn of the macular area, a result of the infra-red rays, and comes on immediately and is permanent. Smoked glasses are used to prevent this in those who wish to look at an eclipse. (*d*) Glare: Almost all of us are made uncomfortable by "glare"; but pathologic lesions produced by "glare" have not yet been found.

The average sun glasses, obtained in drug and ten cent stores, if sufficiently dark, are as a rule comforting to the eyes of the average wearer on an average bright day, on the water or on the beach where they are usually used. They reduce the total amount of light entering the eyes. The idea that certain makes of glass do not transmit the "harmful" ultraviolet light is mostly sales talk, as the ordinary white glass allows but little ultraviolet light to pass through. In fact, in order to obtain passage for ultraviolet through a window pane it has to be specially made for that purpose. A certain amount of ultraviolet light is beneficial to the eyes; it is for this reason that vacations are taken at the seashore and in the mountains, and in the winter patients are sent to sunny climes.

VITAMIN K

To the Editor:—**Is there any danger in the prolonged daily administration of 2 mg. of menadione in a case of intestinal hemorrhage of unknown origin? There is no evidence of prothrombin deficiency. A multiple vitamin capsule includes 10,000 U. S. P. units of vitamin A and 1,000 U. S. P. units of vitamin D. What deleterious effect might be produced by the prolonged administration of one capsule daily in the case referred to?**

M.D., Illinois.

To the Editor:—**For the past two years I have been giving 1 mg. of vitamin K hypodermically to each expectant mother when she goes into labor and also 1 mg. of vitamin K hypodermically to each newborn infant shortly after birth. Is this of any nutritive value and are these dosages correct? Is there any danger in this procedure? Recently detail men have said that vitamin K is now prepared in 5 mg. ampules of 1 cc. each and that this is the proper dose for the type of case described.**

M.D., Texas.

ANSWER.—1. Toxic reactions have not been reported from 2 mg. of menadione daily. It is unlikely that it will be of any benefit if the prothrombin is normal.

The amounts of A and D indicated are well below the toxic level (Park, E. A.: The Therapy of Rickets, THE JOURNAL, Aug. 3, 1940, p. 370. Tumulty, P. A., and Howard, J. E.: Irradiated Ergosterol Poisoning, *ibid.*, May 16, 1942, p. 233) and should not produce adverse effects in the case described in the query. However, the usual preventive dose of vitamin A is 5,000 U. S. P. units daily, being increased to 50,000 daily if evident deficiency exists. One thousand U. S. P. units of vitamin D daily should be adequate for either prevention or treatment in this case.

2. It has been shown beyond any question that vitamin K will correct the hypoprothrombinemia which develops in newborn babies (Quick, A. J.: Vitamin K for the Newborn, THE JOURNAL, March 21, 1942, p. 999) and is probably effective in reducing the incidence and severity of hemorrhages in these babies (Hellman, L. M., and Shettles, L. B.: *South. M. J.* **35**:289 [March] 1942. Williams, R. E.: *Canad. M. A. J.* **52**:397 [April] 1945).

The dosages are correct. It may be desirable to repeat the dose for several days in the babies (Vitamin Deficiencies, THE JOURNAL, June 22, 1946, p. 667). There is no known danger from the procedure.

Harm would probably not result from using 5 mg. doses. Amounts many times this large have been given to adults for considerable periods with insignificant toxic reactions (Allen, J. G.: *Am. J. M. Sc.* **205**:97 [Jan.] 1943. Shapiro, Shepard, and Richards, R. K.: *Ann. Int. Med.* **22**:841 [June] 1945).

DERMATITIS FROM PLAYING CARDS

To the Editor:—What chemicals in the finishing of playing cards might produce a contact dermatitis? John T. Leland, M.D., Mill Valley, Calif.

ANSWER.—The ordinary playing cards are made of paper and stiffened with sizings. Sizings may be any of the natural or synthetic resins or such substances as sodium silicate. Any of the synthetic resins, if they are not completely cured, may cause sensitization dermatitis. Of the natural resins, rosin is the best known sensitizer. Sodium silicate, water-glass, has not been reported as the cause of sensitization dermatitis.

Within the past few years there have appeared on the market washable playing cards which are made of synthetic plastics. If these are incompletely cured they may cause dermatitis, just as may the synthetic resin sizings. In instances in which the dye comes off the playing cards, it is possible that some one may be sensitive to such dyes.

To contract dermatitis from playing cards would be unusual, because contact dermatitis rarely, if ever, occurs on the palms and palmar surfaces of the fingers (places coming in contact with the cards) because of the many layers of cornified epithelial cells covering the true skin in these areas. A diagnosis of dermatitis due to handling playing cards would have to be corroborated by positive patch tests with the playing cards.

ALOPECIA AREATA

To the Editor:—A man aged 44 sought medical care in November 1944 because of a feeling of unusual fatigue and lack of stamina. His doctor prescribed intravenous thiamine hydrochloride injections, daily applications of methyltestosterone, amphetame sulfate (5 mg. twice daily) and vitamin C. About the middle of January 1944 (after about twenty-five applications of methyltestosterone, fifteen amphetame tablets and a number of thiamine injections intravenously) the patient awoke one morning to find his pillow covered with loose hair. On rubbing his face he could feel the stubble of his beard come loose in his hands. After this shocking episode he continued to lose hair from his entire body. In one week there was a complete total alopecia. Since then the patient has been treated by a dermatologist, who prescribed a high acid ash diet and administered roentgen treatments to the scalp (75 roentgens) and grenz ray treatments. He has also received twelve injections of chorionic gonadotropin and a variety of tonics and shampoos, all without effect. Repeated laboratory tests have been normal, including serologic tests for syphilis. The loss of hair has affected the patient's mental state. He borders on desperation unless some relief or hope of relief can be given. Chemical substances which may cause alopecia have been ruled out. Advice as to treatment will be appreciated. M.D., California.

ANSWER.—The patient described in the query has developed a universal alopecia areata. The cause is unknown. The earlier therapy given for the fatigue undoubtedly is not related to the loss of hair. The treatment should be both general and local as well as psychiatric. Wearing a wig helps the patient's morale. The use of tonics and B complex preparations has been recommended. The blood should be examined for the need of hematinics, and any other abnormality of the body should be sought for and corrected. Thyroid has been recommended, as well as agents which are antispasmodics. Local therapy usually includes one or several irritants, but these cannot be employed in this case because of the widespread nature of the ailment. The scalp alone could be treated with them. Liquefied phenol is applied over small areas and quickly neutralized with alcohol.

Generalized exposure to ultraviolet light may be useful in suberythema doses and somewhat larger doses for the scalp. Filtered x-rays to the cervical and other parts of the spine may be tried. The prognosis is poor in these generalized alopecias, especially in a man of middle age.

TENTORIAL TEAR

To the Editor:—How is a tentorial tear resulting from a birth injury diagnosed; and what are the possible sequelae? A diagnosis of "possible tentorial tear" was made at birth in a baby who is now 8 months old. While the entire vault of the cranium has not ossified, the baby appears normal except for an apparent lack of energy. Captain, M. C., A. U. S.

ANSWER.—A positive clinical diagnosis of a tentorial tear is not possible. Such a tear of and by itself is not important, but the hemorrhage and associated cerebral damage may be. The only way in which this can be evaluated is by close observation and examination for evidence of cerebral involvement. The longer a child continues to "appear normal" without evidence of cerebral injury, the less likely does any serious injury at birth become.

TYPHUS IMMUNIZATION FOR PAN AMERICAN HIGHWAY TRIP

To the Editor:—Is it advisable to immunize a person going to Mexico, Central America and South America along the Pan American highway against endemic typhus, epidemic typhus or both?

Regina S. Greenebaum, M.D., Chicago, Ill.

ANSWER.—A person contemplating a trip to the areas mentioned in the query should be vaccinated against epidemic, or louse borne, typhus. Vaccination against endemic, or murine, typhus is not considered necessary.

CHICKEN PICKER'S DERMATITIS

To the Editor:—Several people who are employed at chicken picking have had an eczematoid type of dermatitis involving especially the hand and arm nearest the line of chickens. Please discuss this type of occupational disease. John R. Morrison, M.D., Carroll, Iowa.

ANSWER.—Dermatitis among the handlers of chickens and other types of fowl is not uncommon.

Animal scabies may be contracted from infected domestic fowl. Animal scabies appears as pinhead size papules on the arms, thighs, groin or trunk and sometimes on the face. It may develop in a few hours to two or three days after contact and usually disappears in about three weeks after contact ceases.

Gamasoidosis, or fowl mite disease, is caused by Dermanyssus avium and gallinae. The lesions in man resemble urticarial papules and occur on the hands, forearms, and exposed portions of the neck, chest, and shoulders, and may also involve the face and scalp.

Fowl mites are prevalent on chicken farms. Persons who clean out the coops and those who handle the fowl are attacked by them. The chicken mite Laelaps stabularis may live in stables and attack horses, dogs, and stable men. The parasite may sometimes be seen as dark moving specks on the skin. They do not burrow, but nest in the sweat and sebaceous ducts which gape and become inflamed. This is followed by erythematous exudative folliculitis.

The prevention of the disease consists in wearing impervious sleeves, aprons, and rubber gloves. By applying insect repellents to the workers' clothes and exposed skin and spraying insecticides on the fowl, it may be possible to prevent the disease.

Mixtures of such insecticides and repellents as pyrethrum, DDT, dimethylthalate, Navy insect repellent #448, Indalone, or Rutgers #612 may be used in ointment bases on the skin and in solutions, emulsions or dusts for spraying the fowl.

Reference:

Schwartz, Louis and Tulipan, Louis, Occupational Diseases of the Skin, Philadelphia, Lea & Febiger, 1939, pp. 458-460.

GASTROINTESTINAL DISTURBANCE FOLLOWING MAPHARSEN INJECTION

To the Editor:—The question was asked in Queries and Minor Notes in The Journal, Sept. 14, 1946, page 117, whether there is anything to prevent a gastrointestinal disturbance arising from mapharsen administration. I agree that in a small percentage the psychic factor may play a role. However, in several large clinics which are devoted almost exclusively to the treatment of the Negro race I have seen numerous reactions in which the psychic factor is minimal. I believe that the odor of the drug plays a more prominent role in the gastrointestinal reactions. I have been using ethylaminobenzoate lozenges, following a recently published suggestion. The technic is as follows, with a slight modification: The patient places on the tongue two lozenges, each containing 1/10 grain (65 mg.) of ethylaminobenzoate, one-half hour before the injection is given. This is followed by one lozenge one-half hour after the injection is given. The purpose is to anesthetize the taste bulbs on the tongue. The results have been satisfactory, and few patients have complained of gastrointestinal reaction. I agree that other factors may be contributory.

Meyer L. Niedelman, M.D., Philadelphia.

To the Editor:—In regard to the item in Queries and Minor Notes entitled "Gastrointestinal Disturbances Following Mapharsen Injection" which appeared in The Journal, Sept. 14, 1946, page 117, may I suggest that, while treating a considerable number of servicemen overseas in a venereal disease clinic where for a time we employed mapharsen daily on a twenty day schedule of rapid treatment, this problem frequently arose. Two procedures were adopted which for the most part eliminated the distress of gastrointestinal disturbances in patients who had such reactions: routine administration of atropine sulfate 1/150 grain (0.4 mg.) given one-half to one hour prior to mapharsen therapy, and also the administration of 100 mg. of ascorbic acid three times daily. The latter we felt might in some degree protect against pruritus and the more remote possibility of dermatitis medicamentosa. We never knew whether it did or not, for such reactions did not develop in about 500 cases thus treated with rapid arsenotherapy. At any rate those with gastrointestinal disturbances became few and far between and were usually easily controlled.

Thomas T. Jones, M.D., Durham, N. C.